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A CRITICAL EVALUATION OF MASS ROENTGEN SURVEYS

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One hears in America as well as from England that some mental reservations exist as to the value of mass surveys for the detection of tuberculosis in the light of the long waiting lists of patients with positive sputum.[1] While it is shocking that there is complacency about infectious tuberculosis, there is great virtue in knowing the extent of the problem. The average citizen who finds that he has positive sputum is willing and ready to protect his contacts and to limit his own regimen for the betterment of his health. Thus, the uncovering of cases of active disease results in protection of contacts and, to a limited extent in the absence of adequate facilities, in protection of the patient himself from exacerbation.

However, mass surveys, to be effective in controlling tuberculosis and in uncovering pulmonary neoplasms—their chief values to date—must not be viewed as the mere taking of pictures. In the setting up of units, it must be recognized that more is needed than physical equipment, a technician and a physician-reader. A definite philosophy is required. So far as the reading of the photofluorograms is concerned, they must be overread not underread (fig. 1). The goal is not accurate diagnosis but the screening out of significant or potentially significant pulmonary disease. Because of the infectiousness of pulmonary tuberculosis and the seriousness of bronchogenic carcinoma, all photofluorograms which reveal any of the characteristics of either entity should be read as "suspect tuberculosis" and/or "suspect neoplasm."

Thus a significant percentage of patients whose photofluorograms are considered as showing possible tuberculosis should ultimately be proved nontuberculous. For instance, an area of rarefaction should be interpreted as probably advanced tuberculosis despite the fact that it is later diagnosed as being due to lung abscess. However, no photofluorogram read as nontuberculous basal infiltration, for example, should be found to represent active basal tuberculosis (fig. 2).

Similarly, when a solitary mass, atelectasis, emphysema suggesting obstruction, mediastinal enlargement, soft infiltration or cavity associated with mediastinal shift is found, the survey film should be classified as "suspect neoplasm,"[2] especially in middle-aged men. From Aug. 1, 1948 to April 1, 1949, 0.2 per cent of 43,610 persons surveyed at the Philadelphia Tuberculosis and Health Association were so classified. Neither film reader nor clinician should be disturbed if these lesions are subsequently found to be relatively innocuous. If bronchogenic carcinoma is ever to be conquered, it must be suspected earlier and handled as a medical emergency. Any persistent pulmonary infiltration not definitely diagnosed as tuberculous should be considered potentially malignant for precisely the same reason that it is wise to consider all pleural effusions tuberculous until proved otherwise (fig. 3).

Another important aspect of survey work is the population segment to be studied. While periodic roentgenograms of school children are educational, the yield of significant cases is small. Of 4,059 Philadelphia primary school children surveyed in 1946, only 0.3 per cent were possibly tuberculous. To the time of writing none has been found to have active tuberculosis. In contrast, 8.4 per cent of 3,106 Philadelphia diabetic patients surveyed in 1946 and 2.3 per cent of 32,535 Philadelphia food handlers surveyed in 1947 showed possible tuberculosis. In 1948, 2.5 per cent of 20,903 Philadelphia industrial workers had a survey reading of possible tuberculosis, while for Philadelphia General Hospital admissions and outpatients, as might be anticipated, the percentage was much higher, 6.4.

Great emphasis has been placed on the fact that only apparently healthy persons are suitable candidates for surveys. While this attitude is based on the sound premise that persons with signs or symptoms deserve more careful study than a single miniature film, the fact remains that innumerable persons with symptoms fail to consult physicians but do come to survey units for photofluorograms. Also many physicians, apprehensive about patients who have respiratory symptoms, hesitate to refer them for careful radiologic study because of expense.

If this situation is recognized, a properly indoctrinated survey staff can surmount the obstacles presented by these persons and their physicians in the following manner. The technician can inquire about presence of cough, chest pain and blood spitting as he prepares to take the film. Frequently this elicits voluntary information about other pulmonary symptoms. These data can be noted by the technician on the card so that the physician reading the photofluorograms can add to his "negative" report to the referring physician some such phrase as, "May we call attention to the fact that one miniature photofluorogram does not constitute ade-

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Director of X-ray Surveys, Philadelphia Tuberculosis and Health Association and Division of Tuberculosis, Philadelphia Department of Health (Dr. Boucot) and Associate Professor of Medicine, University of Pennsylvania School of Medicine and Graduate School of Medicine (Dr. Cooper).

1. Time Magazine, Jan. 10, 1949.

2. Boucot, K. R.: Mass Surveys in Case-Finding Techniques for Pulmonary Neoplasms, J. Am. M. Women's A. 3: 12, 485 (Dec.) 1948.

quate study in the presence of signs or symptoms." If such persons have come to community surveys or to stationary units of their own volition, having no private physician, they can be interviewed in the same manner as patients with significant symptoms. An explanation can be made of the importance of more careful studies and suitable referral made.

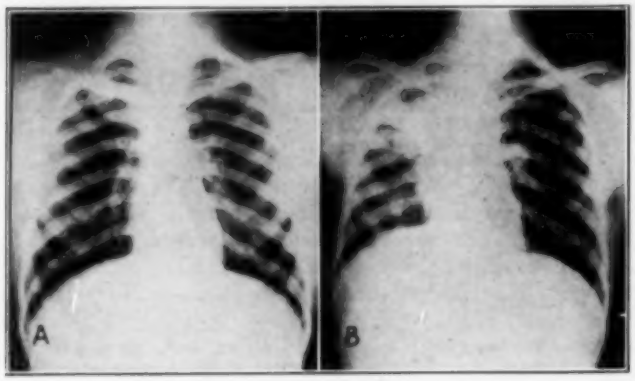

Fig. 1.—Photofluorograms of J. H., an 18 year old white man with diabetes, who on Jan. 18, 1946 was considered "suspect" on the basis of a 70 mm. photofluorogram. The report on a 14 by 17 inch photofluorogram taken February 15 (*A*) read "Minimal, activity indeterminate," and the report on another taken December 30, ten months later (*B*), read "Far advanced tuberculosis with giant cavity occupying most of the upper part of the right lung, dense infiltrations throughout balance of right lung with bronchogenic spread to left second interspace." The photofluorogram revealed early pathologic changes, but the follow-up reflected no confidence in the photofluorographic reading. Lack of suitable clinical study allowed progression to hopeless disease.

There are even a number of ex-sanatorium patients who have not returned to clinics or physicians for years but who come to surveys. We have had patients of that type who had undergone thoracoplasty. These persons should be interviewed, impressed with the wisdom of periodic check-up and referred to a physician or chest clinic. This is a real service the survey unit can undertake. The relapse rate in tuberculosis continues to be about 50 per cent.

Until both the public and the medical profession are better educated, community surveys will be taking miniature films on a significant percentage of persons

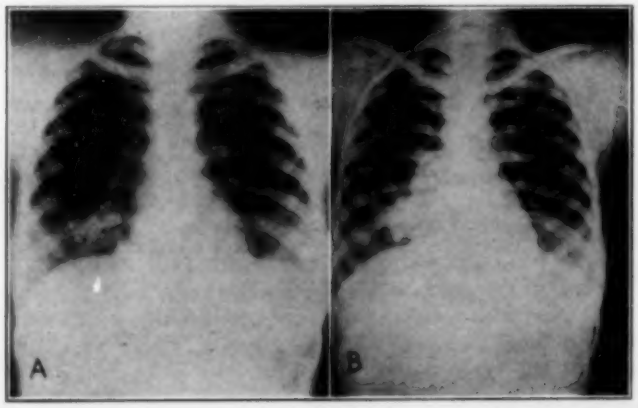

Fig. 2.—Photofluorograms of M. R., a 25 year old white woman with diabetes. The report on a 70 mm. photofluorogram taken April 26, 1946 (*A*) read "Bronchiectasis(?). Infiltrations right base." Another photofluorogram Jan. 31, 1947 (*B*) was taken when the patient was admitted to the Tuberculosis Ward with positive sputum and extension of disease.

with symptoms and/or signs. Should we not become more realistic and set up our work to guard surveys against the fallacies of sending out "negative" notifications to such persons? In industry roentgenograms are made of only 77 to 97 per cent of workers, and, in the percentage failing to report, there are most probably those workers who, being symptomatic, dread discharge from the plant if active disease is found and so fail to report to surveys. Thus, the most important segment in industry may lie in the group failing to report.

Consciously or unconsciously, the United States Public Health Service has recognized this situation and has shifted emphasis from the desirability of industrial surveys to the desirability of community surveys.

Once the readings have been made, prompt interview of the patients with suspected disease is essential. Nonchalance delays processing for weeks or months. Even an intelligent person may not go promptly to a hospital or chest specialist if the suggestion is made weeks after the taking of the photofluorogram. If a film appears to be of grave significance, routine should be discarded and the patient should be sent for at once and, if possible, hospitalized immediately. This means personal effort on the part of the survey physician. Even then it may be too late. Such major decisions and vigorous action cannot be taken by clerks or even by public health nurses. The interview with the patient whose photofluorogram is considered significant should be made by a physician who can explain the photofluorogram to the patient and answer questions authoritatively. Too often unqualified persons strike the same

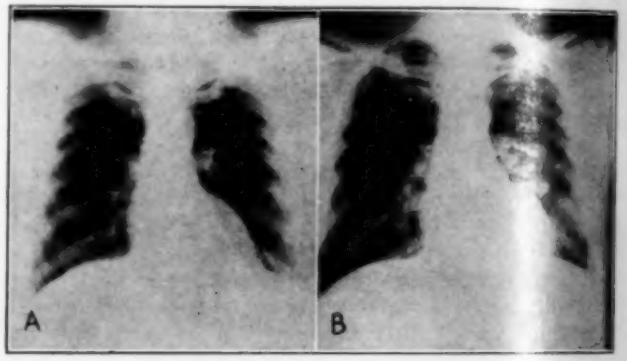

Fig. 3.—Photofluorograms of J. B., a 47 year old white man. The report on a 70 mm. photofluorogram taken Feb. 21, 1947 was (*A*) read "Infiltration right third interspace." Another photofluorogram taken Feb. 4, 1948, one year later (*B*), revealed three rounded masses at the left hilum. The patient refused hospitalization because no symptoms were present. He died seven months later, after hemiparesis. Squamous cell carcinoma of the bronchus with cerebral metastases was revealed at autopsy.

anguish into the heart of a patient with minimal inactive tuberculosis as into the consciousness of a patient with far advanced active disease.

Everything connected with the interview must be done with the greatest consideration. The appointment letter should arrive only the day before the interview in order that anxiety not be prolonged. The appointment letter should not refer to the possibility of pathologic conditions, but should merely state, "Dr. ———— has set aside ——— (date)——— to talk over your x-ray with you." It requires considerable experience to gage the exact approach to persons in order to impress them sufficiently so they will take immediate appropriate action, and yet not produce disproportionate anxiety.

In the early days of our program, patients were referred to their physicians after the interview with the statement that the physician would receive a report. About 20 per cent failed to report to the physician or clinic to which they had stated they would go. By the simple expedient of handing to them a note on which is written their name, the name of the physician or clinic to which they are to go, the date and a brief carefully worded report of survey findings, we obtained

almost 100 per cent response. Like children, with a paper in hand to be delivered, they have some compulsion to complete the job.

Many survey units take 14 by 17 inch (35 by 43 cm.) retake photofluorograms of patients with suspected disease before interview. We began with that policy but abandoned it as a routine when we became convinced of the following contraindications:

1. A single 14 by 17 inch photofluorogram may be no more diagnostic of tuberculosis or bronchogenic carcinoma than a single 70 mm. photofluorogram. That is, what virtue there is in the 14 by 17 inch survey retake lies in the interval of time between the taking of the 70 mm. and the taking of the large film and in projection differences. It is as impossible to make a bacteriologic or a pathologic diagnosis on a single 14 by 17 as on a single 70 mm. photofluorogram.

2. The follow-up is immeasurably delayed unless facilities are available for immediate development of the large film at the time of interview. We find 96 per cent response to our first appointment letter in contrast to 72 per cent response to our first letter requesting the patient's return for a large film. We now take 14 by 17 retakes only in "suspect tuberculosis" or "reserve diagnosis" cases.

The need for proper follow-up is real. Theoretically, once the person reaches the physician or clinic, the survey task has been completed. However, with the press of the urgent needs of patients with symptomatic illness, a significant percentage of clinicians fail to study survey cases adequately. More time and effort are required to convince an asymptomatic patient to be hospitalized than to care for a patient who has reported because he seeks relief. "Gaining weight, no active tuberculosis," "asymptomatic, nontuberculous" and the like are not infrequent replies to routine follow-up questionnaires, even in cases of obviously active tuberculosis. Standards for follow-up examination of survey patients should include at least the taking of serial films and sputum studies, including culture. If sputum is not available and the possibility of activity is real, cultures of the gastric washings should be made. Facilities for tuberculin testing should be available, since it is agreed that, in all but the most exceptional instances, a negative reaction to a tuberculin test done with fresh tuberculin rules out tuberculosis.

It is the responsibility of the survey team to check on follow-up for the sake of the patient, the protection of the community, the education of the physician and the perfection of the survey reader. This is most dramatically obvious in hospital surveys. In most instances, hospital surveys are set up in the Department of Radiology. Reports are sent to the wards or clinics, and there the survey work ends. If the ward physician or clinic physician is alert, appropriate studies and treatment are instituted, but, if no routine to insure such studies is extant, the patient leaves the hospital or fails to return to the clinic and the opportunity for early diagnosis and treatment has been lost. The survey work was merely a gesture.

One last comment needs to be made. Annual roentgenograms of the chest for all adults is a feasible goal. Because of the failure to find bronchogenic carcinoma in a curable stage, we would like to urge that men over age 45 be surveyed every six months.

SUMMARY AND CONCLUSIONS

1. Mass surveys have virtue despite the shortage of beds for tuberculous patients, in that uncovering of infectious cases protects contacts and makes possible the inauguration of a limited type of treatment for the patient himself.

2. Photofluorograms should be overread in order that all persons who could conceivably have pathologic conditions be referred for clinical check-up. The clinicians, understanding this philosophy, should not feel disturbed if his studies reveal no significant disease.

3. Persistent pulmonary pathologic changes not proved tuberculous should be considered potentially malignant, particularly in middle-aged men.

4. While it is desirable that persons with pulmonary signs or symptoms be studied more carefully than can be done by photofluorography, it should be recognized that many symptomatic patients report to surveys. Certain suggestions are made regarding a wiser handling of these patients.

5. The percentage of patients with possible tuberculosis varies with the type of population segment studied —from 0.3 per cent in Philadelphia primary school children to 8.4 per cent in Philadelphia diabetics.

6. A chest specialist is best qualified to interview survey patients with suspected disease. He can authoritatively explain the photofluorogram, answer questions, allay anxiety and arrange for immediate hospitalization in urgent instances.

7. Surveys are merely gestures unless adequate follow-up is an integral part of the survey program.

8. An annual roentgenogram of the chest is advisable for all adults, but men over age 45 should be surveyed every six months.

ABSTRACT OF DISCUSSION

DR. WILLIAM ROEMMICH, Baltimore: Drs. Cooper and Boucot suggest that surveys should be directed toward those population segments with the greatest disease prevalence. They give some strikingly contrasting rates, low for school children and much higher for diabetic, industrial, hospital admission and outpatient groups. These are merely rates of suspected disease based on roentgen findings. I would like to ask them whether there is a direct relation between the rates of suspected disease and active or epidemiologically significant disease, that is, disease which will progress if undetected or which will infect other persons if not properly supervised or isolated. In Minneapolis, where my associates and I did a community-wide survey, there is no direct relation between rates of suspected disease based on roentgen findings and active or epidemiologically significant disease. Drs. Boucot and Cooper also make a plea to include symptomatic persons in mass surveys. I see no serious objection, if symptomatic persons wish to participate in surveys. However, as suggested, these persons need more than roentgen examination. They are already, in many instances, indifferent to persistent cough, chest pain and blood spitting. For these persons the false assurance conveyed by lack of roentgenographic evidence for their symptoms will be a serious disadvantage. They do not understand that affliction of thoracic organs is possible in the face of roentgenograms which repeatedly show apparently normal pulmonary conditions. The authors' suggestion for the handling of symptomatic patients would certainly retard established survey procedure—first, at the screening unit, second, at the film-reading unit and third, in the reporting section. Before such a revision is undertaken I should like to ask if the disease-finding potentiality of the procedure has been measured experimentally in Philadelphia. The authors feel that survey patients with suspected disease should be seen immediately by a physician before a 14 by 17 inch (35 by 43 cm.) confirmatory film is taken. It is not clear to me how a physician seeing a patient with only a 70 mm. film to indicate suspected disease can make a definite diagnosis or allay anxiety. If he will wait a few days for a confirmation, there will be no necessity for him to see some 30 to 50 per cent of these patients, depending on the degree of overreading on the screening film. The confirmatory film alone and a report of normal pulmonary conditions at this time will not

only allay anxiety but, most important, will save the patient time and money and the community valuable professional services sorely needed during survey for those really in need of follow-up.

DR. HERMAN HILLEBOE, Albany, N. Y.: It is recognized in public health, just as in clinical medicine, that there are many different interpretations of the significance of clinical studies. Physicians must not forget that there will be as much variability in the interpretation of the public health technics that are used in the community as there is in the technics used in clinical medicine. The question of overreading is an important problem. Overreading overloads the limited facilities of the survey resources of many communities. Physicians should always strive to be as exact as possible. I think that overreading can often be as dangerous as underreading. When physicians use screening methods, regardless of what size film is used, they are using a dragnet, attempting to catch as many persons with suspected disease as possible. Here, a certain percentage of error can be accepted. When exact diagnosis is being made, then no error that is preventable should be permitted. I think that physicians need to take 14 by 17 inch (35 by 43 cm.) films or many different views, including lateral and oblique views. They must use every means if they are to arrive at an exact diagnosis, and that, of course, is implied in what Drs. Cooper and Boucot said when they pointed out that it is necessary to use the tuberculin test, laboratory studies, history and physical examination. The thing to recall is the base of reference, whether or not one is doing a screening job in discovering persons with suspected disease or whether he is actually attempting to arrive at the diagnosis of tuberculosis. Dr. Roemmich has covered well the first interview and the possibilities of taking a large roentgenogram or not taking it. In order to arrive at the most exact diagnosis possible, physicians should include the large film. To survey the adult population by roentgenogram every twelve months sounds like a good idea, but from the public health viewpoint and in terms of money, priority of other diseases and time it is rarely feasible. I do not think physicians should concern themselves with things they cannot do. Again, physicians must be concerned with whether they are looking for tuberculosis or looking for other diseases and abnormalities as well. If they are looking for tuberculosis, they should survey the adult population group, set up proper control procedures (the examination of contacts, the isolation of patients with infectious disease, the determination of the infection level in the community on an annual basis and the study of death reports as they are recorded) and control tuberculosis in that way.

DR. KATHARINE R. BOUCOT, Philadelphia: In answer to Dr. Roemmich, we do know that, by the most meticulous follow-up in a research project on 500 significant cases, we have had 0.6 per cent clinically active cases of tuberculosis, with 0.3 per cent of these patients actually hospitalized with positive sputum. Routine follow-up on some 30,000 Philadelphia food handlers revealed that 0.25 per cent had been hospitalized or had had hospitalization recommended, while the disease in 0.3 per cent had been judged active clinically. We are aware that even brief questioning regarding symptoms slows the survey procedure, but we view surveys as medical service, not picture-taking. We feel that the responsibility lies squarely on the shoulders of the survey physician to make the project of maximal benefit even though nonroutine questioning takes a few minutes longer than to ask age and marital status alone. As to Dr. Hilleboe's suggestion that overreading overloads the survey follow-up, that is true if the overreading is extreme. Our plan is to consider as "probable tuberculosis" or "suspected neoplasm" such lesions as are definitely seen in the parenchyma. When the question arises whether or not a film shows altogether normal conditions, we consider that it shows only "suspected tuberculosis" and request a large film. Sixty to seventy per cent of cases in the latter category are found to be "negative" on roentgen reexamination, so it is in this small group that we overread. We, too, feel that precision in diagnosis is the realm of the clinician and not the survey physician. As to the ideal viewpoint that annual roentgen check-up is unnecessary if uncovered cases are isolated, the simple answer is that there are not adequate beds available for isolation. In Philadelphia at this moment we have 601 patients on the waiting list. There are probably many more not listed because of the futility of the gesture. Even were this not true, it would take some years to find and isolate all the cases of active tuberculosis because of incomplete population coverage, underreading of films, lack of patient and physician cooperation and the relapsing nature of tuberculosis. We believe annual roentgen check-up is no less feasible than an annual visit to the dentist. We see no need for annual all-out community surveys but feel that, at least in the large cities, existing roentgen facilities would not be overwhelmed by such a recommendation. We would be delighted to see the annual roentgenogram incorporated as a part of the highly desirable annual physical examination.

MASSIVE GASTROINTESTINAL HEMORRHAGE DUE TO JEJUNAL DIVERTICULA

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It may or may not be generally known that over 300 cases of diverticula of the mesenteric portion of the small bowel have been reported in the literature. But that a patient could bleed to death from such a lesion would seem incredible to all except the few who have previously reported this complication. We report this case because it is the seventh of its kind in the literature, it illustrates the seriousness of the hemorrhage that can occur with jejunal diverticula, it furnishes morphologic evidence of this complication and it alerts the general surgeon to the need for more aggressive treatment of patients with massive gastrointestinal bleeding.

REPORT OF A CASE

The patient was a 64 year old white man who, sixteen days before his admisison to St. Francis Hospital in Evanston, Ill., noticed the passage of a large, black, formed stool. This was coincident with his sustaining a fracture of the neck of the left humerus as a result of slipping on ice. The patient's private physician, under whose continuous observation he remained for the sixteen days following the accident, verified the daily occurrence of "tarry" stools. The stools were normal in amount, shape, consistency and lack of pain. To the patient's knowledge he previously never had had "tarry" stools nor had he passed any bright red blood through the rectum. There was no hematemesis or vomiting, no abdominal pain, no change in bowel habit, no flatulence or belching and no gross intolerance to specific foods other than fowl.

Several days prior to his admission to the hospital, the patient had a hematologic study performed, which showed a normal erythrocyte count, leukocyte count, hemoglobin, color index and hematocrit value. Because of apprehension concerning a persistent melena, hospitalization was recommended.

Inventory by systems showed that the patient had dyspnea on exertion in recent years and a chronic nonproducitve cough of several years' duration. His past medical history revealed that he had had congenital syphilis, pneumonia in 1905 and 1944 and typhoid in 1906. The past surgical history included a right sacroiliac strain twenty years previously and a fracture of the left humerus coincident with the onset of the present illness.

All members of the patient's family had died. His father had had diabetes mellitus complicated by a gangrenous toe.

From the Hektoen Institute for Medical Research and the Department of Surgery of the Northwestern University Medical School and of the Cook County Hospital, Chicago, and the St. Francis Hospital, Evanston, Ill.

The mother died of uremia, cause unknown. One brother died of a cardiovascular accident, another of a heart attack and a third of unknown causes. One sister died after a cardiovascular episode.

Physical examination on his entrance to the hospital revealed a well developed, well nourished, white man who was not acutely ill despite his apprehension and appearance of pallor. Though both pupils reacted to light and accommodation, the right pupil was slightly larger than the left. Funduscopic examination gave negative results. The patient had what appeared to be a "saddle-nose" deformity, and there was perforation of the nasal septum. The remainder of the physical examination revealed nothing abnormal except for the presence of "tarry" stools on rectal examination. The blood pressure on his admission was 130 systolic and 80 diastolic. The pulse rate was 76, regular and full. The erythrocyte count made after passage of 500 cc. of "tarry" stools showed 2,650,000 cells per cubic millimeter. The hemoglobin content (Sahli) was 9 Gm. per hundred cubic centimeters. The hematocrit value was 26 per cent. The reaction to the blood Kahn test proved to be 4 plus. Bleeding time was 2 minutes and 52 seconds, and coagulation time was 1 minute and 40 seconds. The total protein concentration was 6.0 Gm. per hundred cubic centimeters; albumin was 3.1 Gm. and globulin 2.9 Gm. The urea nitrogen concentration was 21 mg., and the creatinine was 2.8 mg. The feces gave a 4 plus benzidine reaction for blood.

In view of the absence of a palpable liver or spleen, lack of signs of portal hypertension and lack of evidence to support the diagnosis of a blood dyscrasia, a provisional diagnosis of a bleeding peptic ulcer was made. The patient was given a Mueller's light diet, antispasmodics, vitamins C and K and calcium lactate. He was given 1,000 cc. of whole blood intravenously on the first day.

On the second day the patient passed approximately 1,300 cc. of dark blood through the rectum, his blood pressure averaged 110 systolic and 70 diastolic and he complained of weakness and looked pale. He was given 500 cc. of whole blood and 500 cc. of sodium lactate intravenously. On the third day the red blood cell count was 1,770,000, the hemoglobin content was 5.7 Gm., the blood pressure was 80 systolic and 58 diastolic and the pulse rate was 120 and of poor volume. He passed 1,125 cc. of dark blood through the rectum, and he was given 2,000 cc. of blood and 500 cc. of sodium lactate intravenously during that twenty-four hour period. On the morning of the fourth day his red blood cell count was 3,090,000, the hemoglobin concentration was 8.25 Gm. and the hematocrit value was 33 per cent. He passed 700 cc. of tarry material during the day. After receiving 1,500 cc. of blood that day his blood pressure rose to 130 systolic and 80 diastolic and the pulse rate was 72. On the fifth day the red blood cell count was 3,440,000; the hemoglobin was 11.0 Gm. and the hematocrit value was 30 per cent. He passed 2,700 cc. of dark red blood through the rectum during the ensuing twenty-four hours. During this period he received 1,500 cc. of blood and 500 cc. of sodium lactate. The nonprotein nitrogen was then 39 mg.; the creatinine 2.0 mg.; carbon dioxide–combining power 53 volumes per cent, and the blood chlorides 450 mg. On the morning of the sixth day the patient's blood pressure dropped to 60 systolic and 40 diastolic, and the pulse, though the rate was 68, was poor in quality. He passed 1,350 cc. of blood during the night and had received 1,000 cc. of blood and 200 cc. of dextrose in distilled water intravenously. His erythrocyte count was 2,500,000, the hemoglobin content 7.6 Gm. and the hematocrit 26 per cent.

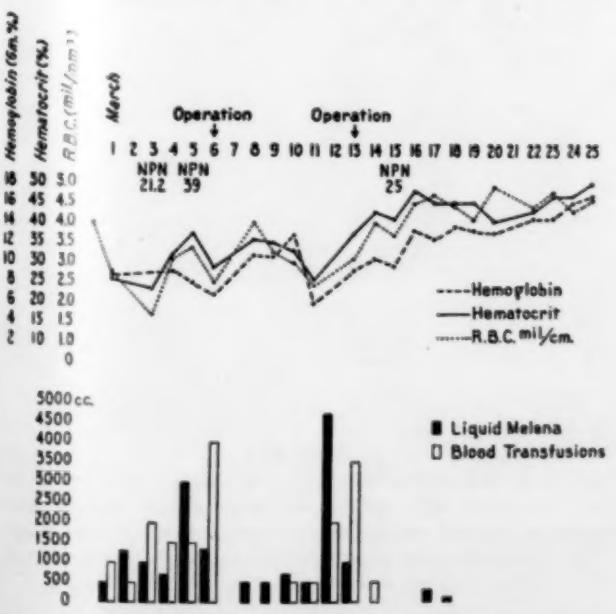

Fig. 1.—Graph illustrating the effect of the blood lost by hemorrhage and of blood transfused on the circulation. A total of 16,600 cc. of blood was passed per rectum whereas a total of 17,500 cc. of blood was administered. Note that final improvement occurred immediately after second operation, which consisted of resection of 51 cm. of jejunum containing multiple diverticula.

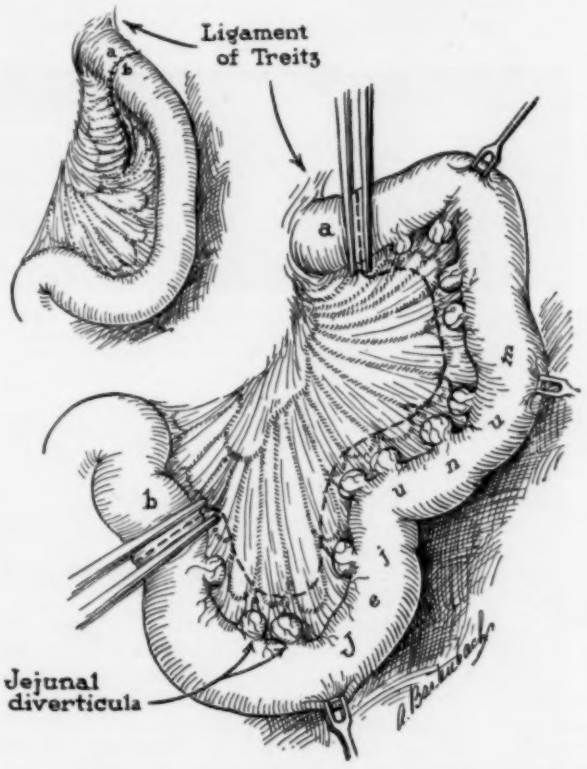

Fig. 2.—Artist's drawing illustrating laparotomy findings. Approximately twelve thumb-sized diverticula bulged between the layers of the mesentery of the jejunum when placed under tension by traction; release of tension resulted in the collapse of the diverticula. The line of resection is indicated by the broken line. The appearance of the anastomosis is shown in the smaller insert.

After medical and surgical consultation a decision was made to explore the patient's abdomen, with the prospect of performing a gastric resection for a bleeding ulcer. The staff roentgenologist felt that a barium meal study at this time would not be reliable enough to yield information of a definite nature. Celiotomy was performed with the patient under intratracheal inhalation anesthesia and was considered to be noncontributory as far as explaining the site of hemorrhage was concerned. The liver appeared grossly normal, there was no evidence of varices, the spleen was of normal size and the stomach and duodenum showed no evidence of ulceration or the presence of a neoplasm. On elevation of the jejunum for careful exploration, several thumb-sized diverticula were seen bulging into the mesentery and immediately collapsed on replacement of the bowel into the peritoneum (fig. 2). On detailed palpation, none of these diverticula felt indurated, nor did they appear to contain any blood. In fact, the entire small bowel was pink and showed none of the discoloration that would

be expected with intraluminal hemorrhage. There were small diverticula in the cecum, descending colon and sigmoid, and the large bowel was slate colored. Because of the lack of awareness that jejunal diverticula could cause massive gastrointestinal bleeding, it was decided to conclude the operation. During the operative procedure the patient received 1,500 cc. of whole blood and 3,000 cc. of 5 per cent dextrose in water. On his return to bed he went into profound shock but responded well to another 1,000 cc. of blood and 1,000 cc. of dextrose.

Fig. 3.—Appearance of the jejunal diverticula after division of the mesentery. Note the thin walls which are traversed by numerous fine blood vessels. The bowel was opened on its antimesenteric border.

The next day (seventh day in the hospital) the patient's systolic pressure varied between 90 and 110 mm. of mercury and the pulse rate was between 60 and 80. There was no melena, and he was given only 2,000 cc. of dextrose solution intravenously and 10 cc. of thromboplastin intramuscularly. The erythrocyte count rose to 4,100,000, the hemoglobin level to 10.5 Gm. and the hematocrit value to 37 per cent. In the next five days the patient again passed 500 to 700 cc. of blood through the rectum daily, and in spite of the administration of another 1,000 cc. of blood the erythrocyte count gradually fell to 2,490,000, the hemoglobin to 6 Gm. and the hematocrit to 24 per cent. It was then decided that further surgical intervention was mandatory, and a plan was proposed to resect the segment of jejunum involved by diverticula and to check the specimen as a source of bleeding. If it did not prove to be the source of hemorrhage, then a gastric resection would be undertaken on empiric grounds.

In preparation for the second operation 2,500 cc. of whole blood was given within twenty-four hours. However, 5,700 cc. of tarry material was passed by the patient from the rectum. The blood pressure at this time was 90 systolic and 60 diastolic, the pulse rate 114, the red blood cell count 3,150,000, the hemoglobin 11 Gm. and the hematocrit 32 per cent.

The second operation was performed on the thirteenth day in the hospital. It was carried out with the patient under intratracheal anesthesia, and a transverse incision was made

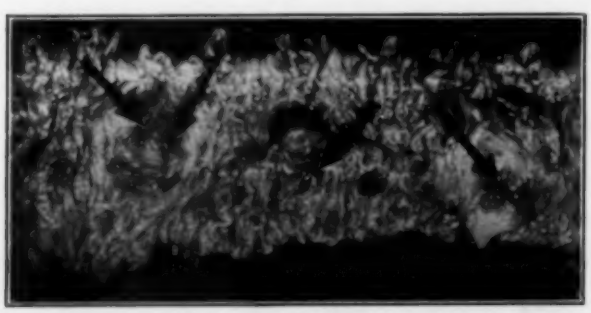

Fig. 4.—Photograph of opened jejunal specimen taken immediately after operation. Arrows point to several mucosal ulcerations varying in size from 2 to 10 mm. Some contain clots of blood. Inflammatory reaction about the ulcer crater was minimal.

because of the previous vertical incision. The findings as shown in figures 2 and 3 were again the same, and an immediate resection of the entire jejunum (51 cm.) with a primary anastomosis of the proximal end (just beyond the ligament of Treitz) to the ileum was carried out as is illustrated in figure 2. The specimen was immediately opened, and when each of at least a dozen diverticula was everted, it was found that approximately half of these contained 2 to 10 mm. mucosal ulcerations and several of them were filled with clotted blood (fig. 4). We then felt confident enough that the source of bleeding was eradicated, and closure of the wound was immediately effected. A 1,000 cc. transfusion of blood was given during the operation and another 1,000 cc. after operation.

The patient tolerated the second procedure remarkably well, and the next morning his blood pressure varied between 150 and 160 systolic and 80 and 90 diastolic. The red blood cell count the day after the bowel resection was 4,000,000, the hemoglobin content 13 Gm. and the hematocrit value 36 per cent. That day he received his thirty-fifth and last transfusion. From then to the time of discharge (twenty-sixth day in the hospital) his course was most uneventful. Except for two small residual tarry stools, the patient soon stopped passing blood per rectum. He maintained a normal hematologic picture (fig. 1), passed brown stools and resumed a normal diet. The patient has now been observed for a period of fifteen months since the jejunal resection, and he is in excellent health. There has been no evidence of recurrent bleeding.

Fig. 5.—Photomicrograph of an ulcer within a jejunal diverticulum. Note that defect in mucosa is filled in by recent and old hemorrhage containing many small blood vessels. Ulcer extends down to muscularis and has incited little inflammatory reaction.

Microscopic study of the surgical specimen was made for us by Dr. Hans Popper, Director of Laboratories of the Cook County Hospital. As is shown in figure 5, the ulcerated area penetrated beyond the mucosa to the muscularis. The ulcer bed was filled with organizing hemorrhagic material which contained several smaller blood vessels. Other areas showed submucosal hemorrhage which had as yet not caused ulceration of the overlying mucosa (fig. 6).

COMMENT

The case has interested us for several reasons. As was stated, it is the seventh case reported to date of jejunal diverticulum complicated by hemorrhage. The first instance of bleeding due to jejunal diverticula appears to be that of Braithwaite in 1924. His patient had symptoms of chronic recurrent obstruction in addition to one emesis of 5 pints (2,500 cc.) of undiluted blood. Resection was performed. In 1930 Somerford discovered such a complication at autopsy. A 7 month old child had severe anemia, melena, emesis and abdomi-

nal pain for two months prior to death. A single jejunal diverticulum was found to be filled with blood. A case was reported by Tengwall in 1931. His patient had recurrent episodes of severe bleeding and anemia until 50 cm. of jejunum was resected. Rankin and Martin cited the case of Haltung, which was that of a 66 year old woman with a roentgenologic diagnosis of jejunal diverticula and tarry stools. Jones and Crile reported their case in 1936. This patient described red blood in her stools on three or four occasions. Guthrie and Hughes reported on a patient with melena, anemia and roentgenologic evidence of jejunal diverticula in 1937.

From the point of view of morphologic evidence of the lesion, this is the fourth case of its kind because 3 of the cases that have been cited as instances of bleeding jejunal diverticula involved patients who had clinical evidence of gastrointestinal bleeding together with roentgenologic evidence of a jejunal diverticulum. In view of the multitude of lesions now reported which may cause bleeding, one could legitimately question those cases lacking anatomic proof of hemorrhage. Fourth or seventh of its kind, it is still a remarkably rare lesion. In conversation with other surgeons during the week between the first and second operations, it was interesting to learn that none of them considered a jejunal diverticulum as the cause of hemorrhage. When one recalls the number of autopsies that have failed to reveal the site of hemorrhage, the error made at the initial laparotomy appears understandable.

The hemorrhage which occurred in this patient seems to be the most severe in the 7 cases now reported. Our patient, by actual measurement, lost 16,600 cc. of tarry material through the rectum. In none of the other cases reported did the loss of blood approach this degree, the closest being that in Braithwaite's case, in which an emesis of 5 pints (2,500 cc.) of undiluted blood was reported. With the exception of Somerford's case (a 7 month baby with necropsy evidence of a bleeding jejunal diverticulum) ours appears to be the most serious from the point of view of a threat to life. None of the adults heretofore reported appears to have gone into shock as a result of the blood loss (considered by many to be one of the criteria for classification as "massive" gastrointestinal hemorrhage). Our patient went into shock on several occasions. The degree of anemia and of dependency on repeated transfusions for sustenance further labels this case as one of massive gastrointestinal bleeding.

The morphologic evidence offered here is rather conclusive, a finding not universal among other similar case reports. Its chief value lies in the possibility that it might suggest another mechanism for the bleeding if not for the diverticulum itself.

The diverticula herein reported are of the acquired type. That is, they occur along the mesenteric border at a point where the intestinal wall is weakened by a perforating blood vessel. (Figure 3 illustrates the large number of fine vessels overlying the surface of the diverticulum.) Fraser considered an additional factor of weakness on the mesenteric border of the jejunum to be the thinness of the longitudinal muscle fibers. Edwards postulated a sudden protrusion of the mucosa through the points of weakness (as with sudden increases in intra-abdominal pressure, such as occur with coughing and sneezing). The history of this patient recalls two possible opportunities for such a development: the chronic nonproductive cough (a postoperative roentgenogram of the chest revealed bilateral bronchiectasis) and the recent trauma, severe enough to have fractured the humerus. Trauma has been considered as sufficient cause for perforation of a previously noninflamed diverticulum; might not trauma then be considered as a possible mechanism for submucosal hemorrhage (as seen in figure 6)? With increase in the size of the submucosal hematoma, secondary ulceration of the thin overlying mucosa may result with exacerbation of the bleeding. In the absence of aberrant pancreatic tissue or gastric mucosa (such as is seen with Meckel's diverticulum) some other mechanism for ulceration must be considered, and the aforementioned hypothesis is offered in lieu of it.

The fluid balance and blood chemistry studies carried out on this patient were detailed and informative (fig. 1). The collection of 16,600 cc. of "tarry" stool

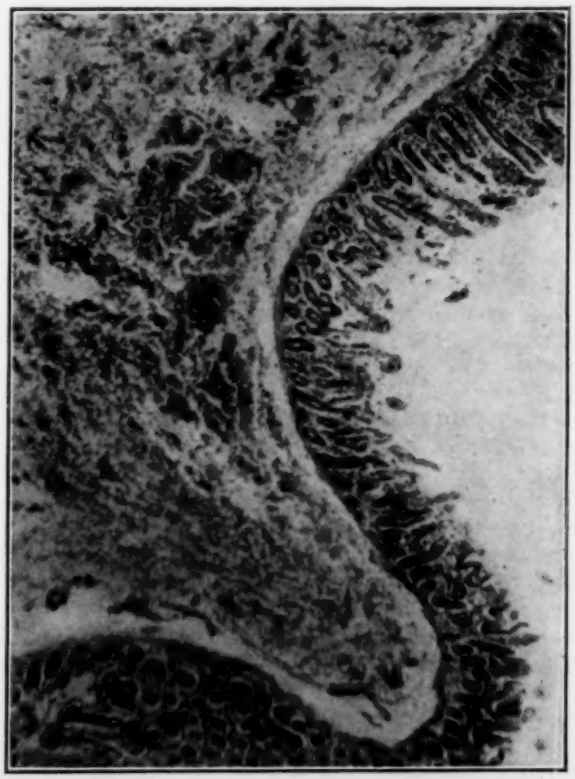

Fig. 6.—Photomicrograph of the wall of a diverticulum illustrating submucosal hemorrhage. It is to be noted that the mucosa is intact. The accumulation of sufficient blood beneath the mucosa is suggested as the mechanism for necrosis and ulceration of the overlying mucosa leading to the type of ulcer and even greater hemorrhage than that seen in figure 5.

is an astonishing figure. If this amount had not been collected, we feel certain that the patient's degree of hemorrhage would have been underestimated. Whether the entire bulk of the material passed by rectum was purely blood is difficult to ascertain, but personal examination by the physicians in attendance indicated that it was principally that. Further evidence that the patient lost approximately this amount of blood is confirmed by the fact that, during the fourteen day period the patient passed 16,600 cc. of this material through the rectum, he required and received 17,500 cc. of whole blood intravenously. In other words, we were just keeping the patient in balance, and we could have used the amount of stool passed as the criteria for the amount needed for transfusion just as well as the red blood cell count, the hemoglobin content, the hematocrit value, the blood pressure and the pulse.

Of biochemical interest is the fact that an extrarenal azotemia never developed, although the quantity of blood lost into the intestinal tract far exceeded that lost by many patients who had shown the rise in urea and nonprotein nitrogen. It at least indicates that these criteria cannot always be depended on to indicate the degree of intestinal bleeding. Possible explanations are the rapid emptying time (indicated by the marked diarrhea and the finding of a pink small bowel at the initial laparotomy) and the care devoted to maintenance of a normal urine output of alkaline character.

Incidentally, another interesting hematologic problem presented itself in this case. The patient's blood type was group 0 and he was Rh negative. He was indigent and without any family or friends who could be called on as donors. Because of his desperate plight it was decided to give him a transfusion with blood in group 0 and Rh positive whenever necessary. Most of his donors were procured as the result of a radio appeal, and thirty-four of the thirty-five transfusions which he received were of the Rh-positive type. There was not a single reaction of even the mildest degree in the entire series of transfusions, and one month after the last transfusion the patient's blood was still Rh negative.

A final item worthy of discussion concerns the need for a more aggressive management of massive gastrointestinal hemorrhage. Jejunal diverticula as a cause of such bleeding will probably not be encountered again in the course of our surgical career, but equally severe hemorrhage from peptic ulcers will. Recent evidence indicates that peptic ulcer is the cause of between 61 and 75 per cent of all cases of gastrointestinal bleeding, and the policy of conservative management of all these merits careful scrutiny. For example, the experience at the Cook County Hospital has been that for persons past the age of 60 the mortality for a bleeding peptic ulcer almost triples that of any previous decade to approach 33 per cent. In addition, the occurrence of shock, red blood cell counts below 2,500,000, repetition of hemorrhage and nitrous retention were all factors which significantly increased the mortality rate. The regrettable experience was that a forty-eight hour interval of conservative trial by the medical department was always permitted before the surgeon was called. Under such conditions, as pointed out by Finsterer in 1939, the mortality rate will be 30 per cent or more. When gastric resection was the operation of choice and was performed within the first twenty-four hours, mortality rates of 5 to 15 per cent have resulted. Before such a program is begun an adequate provision of blood for transfusions must be made. We are certain that the patient on whom we have reported here would not have survived without the availability of a quantity of blood which approximately quadrupled his normal blood volume but barely exceeded his measurable loss.

SUMMARY

1. A case of multiple jejunal diverticula complicated by near-fatal hemorrhage is reported: recovery followed resection of the jejunum. This is the seventh case of its kind in the literature, the fourth case with morphologic evidence of the lesion.

2. The following hypothesis for the development of the lesion in this patient is postulated: The diverticula developed as a result of increased intra-abdominal pressure produced by a chronic nonproductive cough over a period of years. Hemorrhage may have resulted from recent trauma which was severe enough to cause a fracture of the humerus and was coincident to the first occurrence of a bloody bowel movement. The development of a submucosal hemorrhage (fig. 6) to a point where it causes necrosis and ulceration of the overlying thin mucosa (fig. 5) would lead to even greater hemorrhage.

3. Accurate collection of blood lost by rectum can be used as the criteria for blood replacement. In this instance, the 16,600 cc. collected was barely exceeded by the 17,500 cc. administered on the basis of other criteria.

4. The loss of 16,600 cc. of blood into the intestinal tract occurred without development of extrarenal azotemia.

5. A blood group 0, Rh-negative recipient was given one 500 cc. unit of Rh-negative blood and 17,000 cc. of Rh-positive blood without reaction or alteration of his Rh-negative state.

6. The need for earlier resort to surgical methods for the control of massive gastrointestinal bleeding is again emphasized.

POSTCHOLECYSTECTOMY SYNDROMES

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Under the name postcholecystectomy syndromes numerous clinical disorders, which in reality have no relation to the actual removal of the gallbladder, have been reported. However, there is a group of well-defined clinical syndromes which with good reason may be attributed directly or indirectly to some missing functions of the gallbladder and which therefore deserve the name postcholecystectomy syndromes. I believe that the term should be reserved for this group. The following review is based on observations of 1,370 cholecystectomized patients and covers a period of more than 20 years.[1] Some of the patients have been followed five to ten years. In order to avoid the impression of overemphasizing the possible failures and unexpeced sequelae of cholecystectomy and thus obscuring the great and indisputable value of this operation I wish to stress that the 80 per cent excellent results with a mortality as low as 0.5 to 0.9 per cent are not included and discussed in this article. I propose herein to review and summarize many attempts in a longer follow-up to analyze as to the causes of recurrent attacks and various other difficulties in the other 20 per cent of cases. Prediction whether a particular case will belong to the 80 per cent group of complete cures or to the 20 per cent of failures is difficult and makes the problem even more intriguing. These investigations on a larger scale have offered impressive proof that the gallbladder is not a mere nuisance organ like the appendix, which may and actually should be removed whenever it starts to cause trouble. The gallbladder has numerous functions of considerable importance. This fact has not become evident in an impressive way because in about 80 per cent of cholecystectomized persons syndromes of a missing function may never become manifest. In the other 20 per cent they may remain latent until additional damage reveals the weakened functional status of the digestive apparatus and releases the then well-defined clinical syndromes. This additional damage is in most cases due to errors in diet, which in view of the lowered tolerance for food frequently occur.

Surgical Staff, St. Clare's Hospital.

1. Pribram, B. O. C.: Deutsche med. Wchnschr. **55**: 1768, 1929; Les sequelles de la cholecystectomy, Congr. internat., Vichy, 1932; Neue Deutsche Klin. **2**: 165, 1934; Surg., Gynec. & Obst. **60**: 55, 1935.

In the following scheme the main functions of the gallbladder form the basis for analysis and understanding of the real postcholecystectomy syndromes.

Functions related to cholokinesis (expulsion of bile)

1. Regulation of bile pressure in the bile ducts, the gallbladder working as an overflow reservoir and tension bulb

   Clinical syndromes of missing function. Pressure syndromes: cramps in the right upper abdominal quadrant amounting to real colics; nausea and the like

2. Neuroregulation of gallbladder: contraction in relation to opening reflex of the sphincter—

   Clinical syndromes of missing function: dyskinesia of the sphincter—

   (a) Spasm, leading to increased pressure syndromes and biliary stasis, favoring development or flare-up of cholangiohepatitis or pancreatitis

   (b) Paralysis of the sphincter, leading to diarrhea and enteritis

Functions related to biochemical properties of concentrated gallbladder bile

Aid in digestion of food, particularly fat, bile salts and gallbladder hormone (cholecysmon) acting as co-enzymes to the lipases

Clinical syndromes of missing function: lowered tolerance for food, especially fat; anorexia and flatulence

FUNCTIONS OF THE GALLBLADDER

Regulation of Bile Pressure.—When the sphincter is closed either in its normal, rhythmic manner or in an irritable state of spastic contraction the intraductal pressure rises and, provided the cystic duct is patent, the gallbladder fills as an overflow reservoir and acts as a tension bulb. With this regulating mechanism in working condition the intraductal bile pressure is maintained at its normal level of 150 to 200 mm. of water. In case of an occlusion of the cystic duct or a missing gallbladder the unchecked changes of bile pressure, and particularly its rise during digestion and during contraction of the sphincter, are felt by some patients as unpleasant pressure syndromes in the right upper abdominal quadrant. The syndromes may even amount to cramplike pain resembling real gallstone colic. Whether or not these pressure changes are actually felt by an individual patient depends on many additional factors. The width of the common duct is of outstanding importance. Patients with a narrow duct are much more sensitive to pressure changes than those with an enlarged duct. This is certainly the reason why patients who had a simple cholecystolithiasis without involvement of the common duct suffer more frequently with pressure syndromes after removal of the gallbladder than do patients who had a choledocholithiasis with ampullar obstruction, which always involves some dilatation of the common duct. Normally an intraductal pressure to 500 mm. of water is tolerated without any pain. An artificial irritation of the wall of the common duct either through infection or chemical irritants lowers the tolerance for pressure to 100 mm. of water or even less (McGowan, Butsch and Walters [2]). Bearing this in mind one may safely conclude that when an intolerance for increased pressure develops after months or years of tolerance some local inflammatory irritation has developed as an additional damage.

Neuroregulation of Expulsion of Bile.—Not enough attention has been paid to the fact that in total cholecystectomy all the nervous plexuses located in the subserous and muscular layers of the wall of the gallbladder are removed. The nervous impulses originating in these plexuses not only regulate the contraction of the gallbladder but also are intimately connected with the opening reflex of the sphincter which after cholecystectomy is well known to become the uncontrolled and disorderly villain in the play of clinical trouble. The functional status of the biliary tract after complete removal of the gallbladder is quite different from that noted in cases in which a gallbladder clinically is not functioning because of occlusion of the cystic duct. Dyskinetic disorders and spasm may not have been present before operation, but after cholecystectomy such symptoms may develop to a decided degree. It is obvious that spastic conditions developing or becoming exacerbated after cholecystectomy may greatly aggravate the pressure syndromes. Lowered food tolerance in patients subjected to cholecystectomy may easily lead to acute gastroenteritis, in the course of which the first pressure syndromes may appear. Spasm of the sphincter is often the first manifestation of a long-lasting pathologic condition of the biliary duct system eventually involving the liver and pancreas. Such an initial disturbance would be readily counterbalanced by a functioning gallbladder.

The alteration of intraductal pressure following cholecystectomy has been studied in various ways by numerous authors. Naunyn as far back as 1900 measured the intraductal pressure before and after cholecystectomy and found a rise from 25 mm. of mercury to 50 and 55 mm. These observations were later confirmed by all investigators. The influence of drugs on the changes of common duct pressure due to contraction of the sphincter has been studied by several investigators (McGowan, Butsch and Walters,[2] Doubilet and Mulholland [3]). The following observations were made: Morphine injections cause contraction of the sphincter followed by an increase of intraductal pressure from 150 to 200 mm. of water to 250 to 300 mm. Antispasmodics like atropine cause the pressure to drop or at least prevent a rise in pressure after simultaneous administration of morphine. Amyl nitrite inhalation produces a relaxation of the sphincter with an immediate drop of intraductal pressure. Physiologically of special importance is the observation that instillation of hydrochloric acid into the duodenum causes contraction of the sphincter and rise in bile pressure. It is worth bearing in mind that spasm of the sphincter does not cause any pain. The sphincter region is not sensitive, in contradistinction to the region of the opening of the cystic duct, which is highly sensitive. Consequently stones in the common duct, whether lying quietly or passing through the orifice of the duodenal papilla, do not cause any sensation. Pain and discomfort associated with sphincter spasm or stone occlusion are entirely due to the increased intraductal pressure.

SECONDARY POSTCHOLECYSTECTOMY SYNDROMES

Cholangiohepatitis.—Among the complications related to the increased intraductal pressure and stasis of bile (secondary postcholecystectomy syndromes) is cholangiohepatitis.

A woman aged 42 had her gallbladder removed in 1931. Her case was one of simple cholecystolithiasis without disease of the common duct or liver. After a year of complete well-being she began to suffer some recurrent pain and to have

2. McGowan, J. M.; Butsch, W. L., and Walters, W.: Pressure in the Common Bile Duct of Man: Its Relation to Pain Following Cholecystectomy, J. A. M. A. **106**: 2227 (June 27) 1936. Butsch, W. L.; McGowan, J. M., and Walters, W.: Surg., Gynec. & Obst. **63**: 451, 1936.

3. Doubilet, H., and Mulholland, H.: S. Clin. North America, 1949.

a feeling of pressure in the region of the liver. In April 1932 these attacks of pressure were accompanied with fever. Because it was assumed that these syndromes were due to the development of cholangiohepatitis, the patient was subjected to another operation in May 1932. No stones were found in the common duct, and the orifice of the duodenal papilla proved to be patent. The liver was edematous and enlarged. External bile drainage was instituted, whereupon all clinical symptoms subsided. The cholangiogram revealed a sphincter spasm that persisted uninterrupted for twenty minutes. It was promptly relieved by intravenous injection of a solution of 1 mg. atropine sulfate. The drainage tube was removed, and the patient was discharged in good condition without any complaints. After several months of perfect health some of her pressure syndromes reappeared.

Bile pressure and stasis of bile due to spastic conditions of the sphincter often increase after removal of the gallbladder; therefore these incidents of cholangiohepatitis, not present before operation, may rightly be called secondary postcholecystectomy syndromes related to the uncontrolled intraductal bile pressure. Similar conditions prevail in the development of certain forms of pancreatitis.

Pancreatitis.—The relation of pancreatitis to biliary tract disease has long been recognized and established statistically. The question arises whether some chronic and recurrent forms of pancreatitis might also appear as postcholecystectomy syndromes related to sphincter spasm and to increased intraductal pressure. Statistics on the incidence are not yet available, but I have seen impressive examples in patients who for many years had cholecystolithiasis and were under strict medical care. No clinical signs whatsoever were observed that would indicate pancreatic disease. Cholecystectomy was performed, and after a certain interval, again usually following some indiscretions in diet, definite signs of pancreatic disorders appeared, such as pain and cramps in the epigastrium and diarrhea with increase of undigested fat in the stool. In recent cholangiographic studies carried out by Doubilet and Mulholland [3] the importance of an open pathway between the common and the pancreatic duct plus the incidence of sphincter spasm favoring the reflux of bile into the pancreatic duct has been well illustrated. With the increased possibility of reflux of bile into the pancreatic duct because of sphincter spasm, some pancreatic disorders (edema or fibrosis) might well develop as sequelae of the increased bile duct pressure following removal of the gallbladder as a tension bulb organ.

However, there are cases in which pancreatic conditions related to biliary tract disease disappeared dramatically after cholecystectomy. This is not surprising. Reflux of bile into the pancreatic duct constitutes only one and probably not even the most common cause in the pathogenesis of pancreatitis. I have observed instances in which autopsy proved in a convincing manner that infection of the gallbladder had spread to the pancreas by way of the lymphatic vessels. Animal experiments carried out by Graham [4] offered good support for these observations in human disease states.

Atony or Paralysis of the Sphincter.—Spastic contraction of the sphincter following cholecystectomy occurs only in a certain group of patients. In others a pronounced atony or even complete paralysis follows the removal of all the nervous plexuses when cholecystectomy is performed. This fact has been established by numerous authors in animal experiments. Oddi as far back as 1888 observed in dogs a permanent drainage of bile into the duodenum causing severe diarrhea. Judd and Mann in measuring the intraductal pressure after cholecystectomy recorded in some instances, following an initial rise, a gradual diminution of pressure to zero, indicating the development of total paralysis of the sphincter. This means a continuous drainage of bile into the duodenum instead of the rhythmic and interrupted emptying regulated by a functioning sphincter and related to the contraction of the gallbladder. Continuous drainage of bile into the duodenum, particularly when the patient is in a fasting state, may be followed by a complexity of clinical syndromes with diarrhea and other digestive disturbances predominant. Such diarrhea may be due merely to the purgative effect of the excess of bile salts pouring continuously into the duodenum. However, there is also a real gastroenteritis and particularly duodenitis observed, which deserves full attention. Such a duodenitis may be the cause of serious trouble to the patient long after cholecystectomy, when his previous gallstone disease is almost forgotten. This fact and the actual cause of this diarrhea, as well as the good chance of obtaining dramatic results with adequate treatment—hydrochloric acid and pepsin in large doses—are not common knowledge. Apart from these more chronic forms of diarrhea as late postcholecystectomy syndromes, fulminant forms of diarrhea, although rare, are observed in the early postoperative course, some even leading to fatal issue.

Cholecystectomy for simple cholecystolithiasis without occlusion of the cystic duct was performed on a woman aged 34. The operation was simple, and there were no complications. The abdominal wall was closed without drainage. On the second postoperative day profuse diarrhea began with dark, foul-smelling stools. In the next few days the diarrhea increased with up to fifteen stools a day. The temperature rose to 102 or 103 F. The patient's condition deteriorated in spite of energetic supportive therapy and fluid replacement. She died on the seventh postoperative day. At autopsy the operative field was dry and showed no inflammation. The peritoneum was pale, and the only pathologic condition was acute duodenitis and enteritis.

In about 1,500 cholecystectomies I have seen 5 similar cases with 2 fatalities. Bacteriologic examination showed Escherichia coli in cultures in 4 cases and Salmonella paratyphoid B in 1 case. Such cases are certainly rare, and the pathogenetic explanation is not clear. However, the relation to cholecystectomy (probably followed in these cases by paralysis of the sphincter) is indisputable. The continuous flow of infected bile probably caused the duodenitis and jejunitis. These cases resemble in a striking way those observed by Oddi in cholecystectomized dogs.

SYNDROMES OF THE MISSING BIOCHEMICAL FUNCTIONS OF THE GALLBLADDER

The biochemical functions of the gallbladder are twofold: (1) the concentration of bile, which increases its digestive aid, and (2) the secretion of a hormone-like substance named cholecysmon with the properties of a co-enzyme in activating the fat-splitting lipases.

Concentration of Bile.—Concentrated bile with its salts is an important aid in the digestion of food. Bile salts activate digestive enzymes, form conjugated products with poorly soluble and therefore poorly absorbable substances, and help the latter to pass through the intestinal wall into the blood and lymph stream. The bile salts act as catalysts both in the breaking down and in the absorption of foodstuffs. The gallbladder empties the highly efficient concentrated bile by active contrac-

4. Graham, E. A.: Diseases of the Gallbladder, Philadelphia, Lea & Febiger, 1927.

tion in response to the stimulation of food during digestion and the formation of cholecystokinin in the intestines.

Secretion of Activator Substance.—The gallbladder wall produces a substance, cholecysmon, which is a specific activator for the fat-splitting lipases. The existence of this activator in the wall of the gallbladder has been proved by simple experiments:

1. Under normal conditions neither liver bile nor gallbladder bile has any fat-splitting functions. The bile contains only substances which act as co-enzymes in activating and increasing the digestive titer of the lipases.

2. This effect is greater in the concentrated gallbladder bile than in the diluted liver bile. However, when gallbladder bile was diluted to contain the same amount of bilirubin as liver bile (measured by colorimetric tests), the activating power remained greater in the gallbladder bile than in the liver bile (figs. 1 and 2). Hence, the conclusion must be drawn that the composition of the gallbladder bile differs from that of the liver bile not only quantitatively but qualitatively: the wall of the gallbladder probably produces another specific activator that is either entirely absent in the

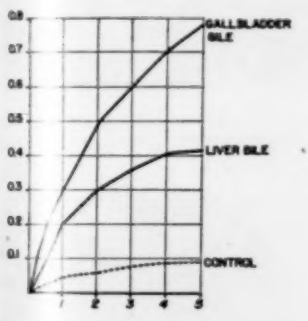

Fig. 1

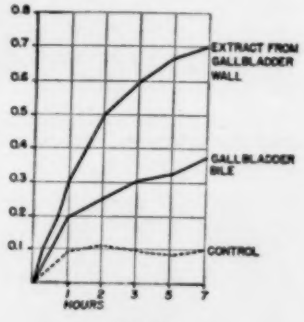

Fig. 2

Fig. 1.—Curve showing the comparative activating of lipases and enzymes by extract from gallbladder wall and gallbladder bile.

Fig. 2.—Curve showing the comparative activating of lipases and enzymes by gallbladder bile and liver bile.

liver bile or present in much smaller quantities. Furthermore, this activator cannot belong to the group of bile salts, which are all excreted by the liver and present in the liver bile. These primary conclusions have been fully confirmed by further investigations. This substance acts not only when brought in direct contact with the pancreatic lipases by oral administration but with even better effect when given by parenteral injection. Consequently, this substance is not a mere digestive adjuvant, like pepsin, hydrochloric acid or pancreatic amylase and trypsin. It apparently behaves more like a hormone influencing the metabolism of fat. It acts as a co-enzyme not only for the pancreatic lipases but for other intracellular fat-splitting enzymes as well. This observation explains the effect of its parenteral injection. The lack of these biochemical functions in cholecystectomized patients may well account for the almost constantly observed lowered tolerance for food, especially fatty food. Therapeutically cholecysmon has proved exceedingly valuable in the treatment of postcholecystectomy syndromes related to digestive disorders.

PREVENTION OF POSTCHOLECYSTECTOMY SYNDROMES

Conservative Operation.—Considering the important functions of gallbladder, the absence of which in patients subjected to cholecystectomy may account for many distressing and serious clinical syndromes, an attempt seems to be justified to preserve in suitable cases a still functioning gallbladder and to restore its damaged function instead of removing the whole organ. Stasis of bile in the gallbladder and difficulties in emptying form the basic pathologic conditions on which most cholecystic diseases, including the formation of stones, develop. Consequently, the given aim of a conservative operation would be the relief of stasis and the securing of free drainage from the gallbladder into the common duct. This can be done in performing a shunt operation under the obstacle-forming cystic duct system, i. e., an anastomosis between gallbladder and common duct, a cholecystocholedochostomy.[5] In this way preservation of the tension bulb function of the gallbladder and also of its secretory activity may well be expected. In contradistinction to a cholecystoduodenostomy, which should not be considered for this purpose, the sterility of the gallbladder, if present, can be preserved and the danger of an ascending infection avoided. Furthermore, the physiologic function of the sphincter of Oddi in regulating the rhythmic flow of bile into the intestines is also preserved. The ill effects of spastic conditions, should they occur, are well counterbalanced by the restored tension bulb function of the gallbladder. The technic of the operation presents no difficulty. It can be performed also on a narrow common duct. Figure 3 illustrates the procedure. The anastomosis can be made over a rubber tube or without it.

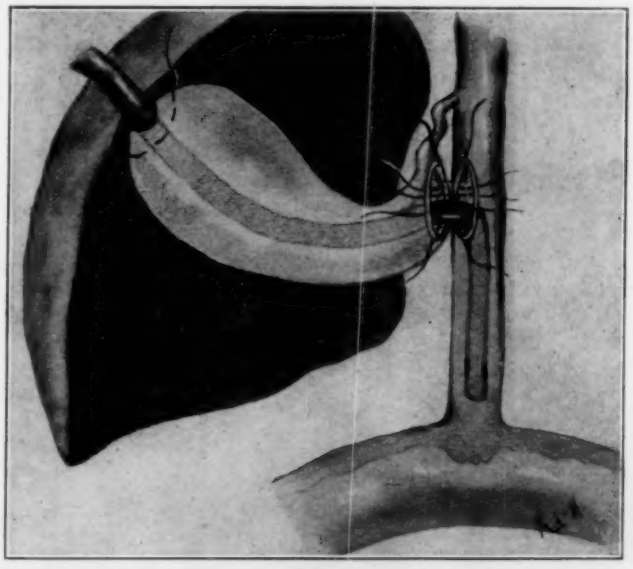

Fig. 3.—Technic of cholecystocholedochostomy.

Results.—I have performed the shunt operation on 36 patients to date. One patient died with pneumonia, 2 have undergone reoperation for pain persisting after six months. Cholecystectomy was performed but failed to relieve the patients of their symptoms, which were probably due to chronic fibrotic pancreatitis. In the remaining 33 cases the results were good, and in the majority excellent. In no instance has colic or even milder pressure syndromes been observed in a follow-up of three to five years. The tolerance for food was considerably improved, and in many instances the patients no longer had to observe dietary restrictions. This

5. Pribram, B. O. C.: München. med. Wchnschr. **46**: 1823, 1935; Zentrabl. f. Chir. **60**: 1506, 1933; Surg., Gynec., & Obst. **60**: 55, 1935; Lancet **1**: 69, 1940; J. Internat. Coll. Surgeons **10**: 3, 1947; Congr. Internat. Vichy, 1937.

improvement of tolerance for food has been striking in the early postoperative course. In contrast to the usual anorexia, after cholecystotomy many of these patients with conservative surgical operation had a ravenous appetite. Moreover, they developed fancies for special food and indeed became veritable gourmets. Two questions have to be answered: First, does the anastomosis remain patent? Six months after operation a woman aged 28 had an appendectomy. During this operation iodized oil (lipiodol®) was injected into the gallbladder and a roentgenogram was taken (fig. 4). The gallbladder shows a normal outline and a wide open anastomosis. Second, is the gallbladder able to empty its content? A roentgenogram (fig. 5) shows the lipiodol®-filled gallbladder of another patient emptying through the anastomosis one week after operation. The emptying was complete within twelve hours.

Indications.—Since the postcholecystectomy syndromes, especially the pressure syndromes, appear only in about 20 per cent of patients subjected to cholecystectomy it is important to know how one may diagnose the condition or recognize in advance those patients in whom the syndromes are likely to develop. Certain tendencies may be noted. Young women with signs of (1) pronounced irritability of the vegetative nervous system, especially the digestive apparatus, (2) a tendency to spasm and (3) hyperacidity and constipation of a spastic type constitute the majority of those in whom pressure syndromes are likely to appear after removal of the gallbladder. In my series these observations have been clearly defined: low incidence of postcholecystectomy syndromes in complicated cases and relatively high incidence in cases in which cholecystectomy has been performed in the presence of a not too badly damaged and still somewhat functioning gallbladder. The diagnosis of a still functioning gallbladder can be made clinically and roentgenologically only when the cystic duct is patent. However, roentgenographic demonstration of occlusion of the cystic duct is no proof that the gallbladder wall is damaged beyond hope of functional repair. A small stone might have slipped into the cystic duct; after removal of the stone and restoration of free drainage the gallbladder may recover completely. However, the actual decision whether a gallbladder has to be removed or an attempt may be made to perform the conservative cholecystocholedochostomy can be made only at operation by exploration

Fig. 4.—Gallbladder lipiodol® filling six months after cholecystocholedochostomy.

Fig. 5.—Gallbladder lipiodol® filling emptying through anastomosis six days after cholecystocholedochostomy (one hour after filling).

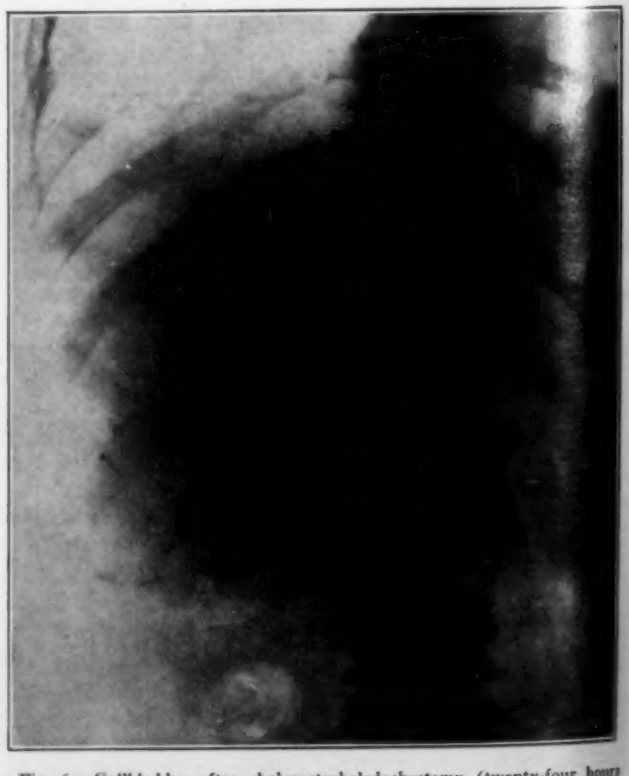

Fig. 6.—Gallbladder after cholecystocholedochostomy (twenty-four hours after filling) emptying through anastomosis.

of the site. In the beginning I confined the operation only to cases of dyskinesia and roentgenologically proved difficulties in the emptying of a static gallbladder. However, encouraged by the favorable results I performed the operation also in the presence of some faceted stones, provided the wall of the gallbladder was not seriously damaged and some contractility could be expected. The results suggest that securing of free drainage and prevention of stasis give mild inflammation a fair chance to subside and prevent new formation of stones, which in no instance has been observed.

TREATMENT OF POSTCHOLECYSTECTOMY SYNDROMES

Most of the troublesome postcholecystectomy syndromes are directly or indirectly related to the abnormal intraductal bile pressure; hence the relief of these conditions has to be the main object of treatment. The truth of this concept has been proved by the well-established observation that in securing free drainage of bile, thus relieving the intraductal pressure and preventing biliary stasis, all the secondary syndromes related to these primary conditions, such as flare-ups of cholangiohepatitis or pancreatitis, likewise may disappear in a dramatic way.

Medical Treatment.—Medical treatment of postcholecystectomy syndromes is successful in many instances. The main principle in preventing sphincter spasm and pressure syndromes is correct diet. All irritants known to cause spasm, such as fatty food, iced drinks, foods that increase gastric acidity, like coffee or alcoholic beverages, should be strictly avoided. Since hydrochloric acid has a decided stimulating effect on sphincter contraction antiacid therapy is one of the chief aims of any dietetic regimen. All spicy food has to be avoided, use of salt has to be restricted and in addition alkalies should be administered regularly after meals. Antispasmodic drug therapy has yielded disappointing results. However, belladonna and papaverine may be useful for their inhibiting action on gastric secretion. Morphine, if necessary, should never be given without an adequate dose of atropine sulfate (1 mg.). In case of paralysis of the sphincter followed by diarrhea dramatic effect may be obtained by the administration of hydrochloric acid and pepsin in sufficient doses after each meal. If medical treatment fails, and especially if secondary complications such as fever indicate the development of cholangiohepatitis, surgical treatment should not be delayed.

Surgical Treatment.—The following surgical procedures are at one's disposal and choice: 1. External Biliary Drainage: The most drastic method is external drainage of bile, which is imperative in cases of cholangiohepatitis with fever. It is also the safest method to use in dealing with more acute flare-ups of pancreatitis. External drainage should be maintained for at least six weeks. A cholangiogram must always be taken in order to visualize the duodenal papilla and to make sure that stones are not present and responsible for the back pressure and biliary stasis. If stones are discovered they are dealt with by the ether method.

2. Choledochoduodenostomy: The idea behind choledochoduodenostomy is to short-circuit the spastic orifice of the duodenal papilla and to secure unimpaired drainage of bile into the duodenum. Considerable experience has been gained with this method over more than forty years. The results may be summarized as follows: Favorable statistics have been reported by numerous surgeons, especially from the European Continent.[6] The main objection to this operation is the danger of an ascending infection of the biliary tract. Reflux of duodenal contents into the common duct is observed almost regularly. However, the danger of development of a clinical cholangitis is slight provided the anastomosis is made wide enough to secure free drainage and to prevent any blocking by duodenal contents, should they enter the anastomosis. I have records of patients followed for more than eight years. In all of them reflux of barium sulfate meal into the common and even intrahepatic ducts has been observed on roentgen examination. However, clinical cholangitis did not develop in any of them.

3. Methods of Severing the Sphincter: Choledochoduodenostomia interna: The musculature of the sphincter is dissected from a transduodenal incision. Doubilet and Mullholland recently reported 3 cases of chronic pancreatitis originating in a biliary reflux through a common pathway into the pancreatic duct. Section of the sphincter brought relief of all pancreatic syndromes. These observations constitute an impressive support of the concept of the importance of sphincter spasm in the pathogenesis of some forms of pancreatitis.

Paravertebral Block: This therapeutic procedure is based on the observation that dissection or anesthetic block of the paravertebral ganglions causes relaxation of the sphincter and increase of bile flow. Procaine hydrochloride, 25 cc. of a 1.5 per cent solution, is injected at the site of the paravertebral ganglions between the tenth and twelfth dorsal vertebrae. The few personal experiences I have had with this method have been encouraging, and I feel justified in recommending that this simple and harmless method be tried before major surgical intervention is contemplated.

Sympathectomy: Experience with sympathectomy for relieving pressure syndromes in the biliary tract is at present too limited to permit any evaluation. If paravertebral block yields good but only temporary results, this may be taken as an indication that sympathectomy would probably have the desired and lasting effect.

SUMMARY

A group of clinical syndromes is described which deserve the name postcholecystectomy syndromes. These syndromes can reasonably be considered due to some missing functions of the gallbladder. The main syndromes are:

1. The pressure syndromes due to the missing tension bulb function of the gallbladder and their secondary complications, cholangiohepatitis and pancreatitis.

2. The lowered tolerance for food, especially fatty food, due to the missing digestive aid of concentrated gallbladder bile and the hormone secreted from the wall of the gallbladder.

3. Paralysis of the sphincter, leading to diarrhea and enteritis.

Cholecystocholedochostomy is described and recommended as a conservative surgical method for preserving the main functions of the gallbladder in suitable cases instead of removal of the whole organ. Conservative and surgical methods for treatment of postcholecystectomy syndromes are discussed.

910 Fifth Avenue (21).

6. Mallet-Guy, and Marion: Rev. du foie **3**: 217, 1940.

SUDDEN DEATH DURING CHILDHOOD WITH XANTHOMA TUBEROSUM

Review of Literature and Report of a Case

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Cardiac disease associated with xanthoma tuberosum has been observed [1]; however, the occurrence during childhood is infrequent. Cook and associates [2] in 1947 collected from the literature 20 cases of xanthoma tuberosum in patients 31 years of age or less who had either definite or probably associated heart disease. Only 13 of this group were 16 years of age or younger when first observed to have cardiovascular lesions.[3] The case of Cook and associates,[2] the 2 cases reported by Montgomery and Osterberg [1b] and McGraw [4] bring the number to 17. Sudden death is known to have occurred in 6 of these cases.[5] An autopsy was performed in only 2.[5a]

Six cases of sudden cardiac death in children 16 years of age or younger with autopsy have been reported as resulting from arteriosclerosis.[6] Since the clinical observations and the visceral lesions are similar, whether or not xanthomas are present, the observations in the 8 cases with autopsy will be considered together in this review.

The clinical and pathologic observations in xanthoma tuberosum have been discussed elsewhere.[7] The tumors may vary in both size and anatomic location. Usually they are yellow and are found in the subcutaneous tissue around the elbows, knees and buttocks and attached to tendon sheaths. The lipoid-holding cells may or may not be accompanied with giant cells.[8] The etiologic basis of xanthomatosis is not known despite discussion.[9] Thannhauser and Magendantz [10] have classified xanthomas primarily as hypercholesteremic and normocholesteremic, although some cases have certain features of both types. The hereditary manifestations of xanthomas have been recognized for many years.[11] Gossage [12] expressed the belief that xanthomas are inherited through a single dominant factor.

All xanthomas occurring in the subcutaneous tissue or attached to tendon sheaths in children apparently are not accompanied with cardiovascular lesions [13]; cases of sudden death in children may result from arteriosclerosis without xanthomas.[6] Xanthoma tuberosum with sudden cardiac death also occurs during adult life. In these adult cases the association of arteriosclerosis and the familial tendency to xanthomas similar to that observed during adolescence [14] has been noted. Several reports of arteriosclerosis and sudden death in young adult males have been made since the last war.[15]

REVIEW OF CASES IN THE LITERATURE

A summary of the clinical and pathologic observations in the 2 cases of xanthoma with sudden death and the 6 cases of arteriosclerosis with sudden death in children 16 years of age or younger previously reported by others are as follows:

CASE 1.[2]—A white boy 13 years of age had xanthomas about the elbows, fingers, knees, ankles and toes, with a history of dyspnea and substernal pain on exertion. A systolic precardial murmur was heard best over the aortic area, and it was transmitted to the large vessels in the neck. The blood pressure was 132 systolic and 84 diastolic and the pulse rate was 104 per minute. An electrocardiogram showed inverted T waves in leads 3, 4_F and 4_R. The determination of blood cholesterol was 561 mg., cholesterol esters 360 mg., total fatty acids 948 mg., lipids 1,509 mg. and lecithin 496 mg., per hundred cubic centimeters. The sedimentation rate was 43 mm. per hour (Westergren). The patient died a sudden cardiac death.

At necropsy the cusps of the aortic valve were thickened and fibrotic, producing a moderate amount of insufficiency. There was grade 1 arteriosclerosis of the mitral valve. The coronary arteries showed grade 3 sclerosis with focal areas of extensive yellowish deposits and slight calcification. The orifice and lumen of these vessels were narrowed, especially those of the anterior descending branch of the left coronary. Many of the fibers in the myocardium were filled with fine fat globules. The aorta showed enormous plaques formed by fibrous tissue and calcium. The media and intima were infiltrated by groups of lymphocytes. The subcutaneous tumors were typical xanthomas.

Anatomic diagnoses were: xanthoma tuberosum multiplex; coronary sclerosis, grade 3, with pronounced narrowing of the anterior descending branch; infarct of the left ventricle (anterior wall), and arteriosclerosis, grade 3, of the aorta.

CASE 2.[3b]—A white girl 11 years of age had xanthomatous lesions in the subcutaneous tissue of the elbows, buttocks, knees and feet, and similar tumors were attached to the extensor tendons of the fingers and to the achilles tendons. The heart was enlarged, and there was a systolic murmur at the apex. The child was seized with palpitation and breathlessness and died within twenty-four hours. At the postmortem examination

From the Department of Pathology, University of Texas Medical Branch.

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2. Cook, C. D.; Smith, H. L.; Giesen, C. W., and Berdez, G. L.: Xanthoma Tuberosum, Aortic Stenosis, Coronary Sclerosis, Angina Pectoris, Am. J. Dis. Child. **73**: 326 (March) 1947.

3. (a) Poenagen, A.: Mittheilung unis seltmen Falles von Xantholasma Multiplex, Virchows. Arch. path. Anat. **91**: 350, 1883. (b) Lehzen, G., and Knauss, K.: Ueber Xanthoma Multiplex, planum, tuberosum, Mallusciforme, ibid. **116**: 85, 1889. (c) Low, C. R.: Xanthoma Tuberosum Multiplex with Lesions in the Heart and Tendon Sheaths, Brit. J. Dermat. **22**: 109, 1910. (d) Arning, E.: Ein Fall von Familiarer Xanthomatose, Arch. Dermat. u. Syph. **105**: 290, 1910. (e) Knowles, F. C., and Fisher, H. N.: Xanthoma Tuberosum Multiplex in Childhood with Visceral and Tendon Sheath Involvement, J. A. M. A. **77**: 1557 (Nov. 12) 1921. Lapowaski: Familial Xanthoma Tuberosum Multiplex in Two Sisters, Arch. Dermat. & Syph. **11**: 701 (May) 1925. (f) Lane, C. G., and Goodman, J., Jr.: Xanthoma Tuberosum: Report of Familial Occurrence with Probably Cardiac Lesions, ibid. **32**: 377 (Sept.) 1935. (g) Bloom, D.; Kaufmann, S. R., and Stevens, R. A.: Heredity and Xanthomatosis, ibid. **45**: 1 (Jan.) 1942. (h) Gwynne, C. N.: Rep. Soc. Study of Dis. Child. **5**: 318, 1905; cited by Cook.[2]

4. McGraw, A. B.: Juvenile Xanthoma Multiplex: Case Report and Discussion of Literature, Am. J. Cancer **18**: 345, 1933.

5. (a) Cook, Smith, Giesen and Berdez.[2] Lehzen and Knauss.[3b] (b) Arning.[3d] Bloom, Kaufmann and Stevens.[3g] Gwynne.[3h]

6. (a) Benda, C.: Ueber einen Fall von Schwerer Infantile Karonararterien-Sklerose als Todesursache, Virchows. Arch. path. Anat. **254**: 600, 1925. (b) Sprague, H. B., and Orgain, E. S.: Electro-Cardiographic Study of Cases of Coronary Occlusion Proved at Autopsy at the Massachusetts General Hospital 1914-1934, New England J. Med. **212**: 903, 1935. (c) Wild, R. B.: A Contribution to the Pathology of the Coronary Arteries, M. Chron. **16**: 223, 1892. (d) Jokl, E., and Greenstein, J.: Fatal Coronary Sclerosis in a Boy Ten Years, Lancet **2**: 659, 1944. (e) Dreschfeld, J.: On Angina Pectoris and Pseudo-Angina, Practitioner **44**: 32, 1890.

7. Montgomery and Osterberg.[1b] Bloom, Kaufmann and Stevens.[3g]

8. (a) Hess, F. O.: Ueber allegemeine Xanthomatose, Verhandl. d. Deutsch. Gesellsch. f. inn. Med. (Kong. 461) 1934, p. 355; München. med. Wchnschr. **81**: 579, 1934. (b) Beeson, B. B., and Albrecht, P. G.: A Contribution to the Study of Xanthoma Tuberosum with Report of a Case, Arch. Dermat. & Syph. **8**: 695 (Nov.) 1923. Footnote 7.

9. Müller, C.: Angina Pectoris in Hereditary Xanthomatosis, Arch. Int. Med. **64**: 675 (Oct.) 1939. Footnote 7.

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11. (a) Török, L.: De la nature des xanthomes avec quelques remarques critiques sur la notion des tumeurs, Ann. de dermat. et syph. **4**: 1109, 1893. (b) Boas, E. P., and Aldersberg, D.: Familial Hypercholesterolemia and Atherosclerosis, J. Mt. Sinai Hosp. **13**: 84, 1945. (c) Bloom, Kaufmann and Stevens.[3g]

12. Gossage, A. M.: The Inheritance of Certain Human Abnormalities, Quart. J. Med. **1**: 331, 1908.

13. Harblitz, F.: Tumors of Tendon Sheaths, Joint Capsules and Multiple Xanthoma, Arch. Path. **4**: 507 (Oct.) 1927. Weidman, F. D., and Freeman, W.: Xanthoma Tuberosum, Arch. Dermat. & Syph. **9**: 149 (Feb.) 1924.

14. Lane and Goodman.[3f] Boas and Aldersberg.[11b]

15. Engleberg, H., and Newman, B. A.: Xanthomatosis: A Cause of Coronary Artery Disease in Young Adults, J. A. M. A. **122**: 1167 (Aug. 21) 1943. Tullis, J. L.: Coronary Thrombosis in Youth, U. S. Nav. Bull. **45**: 334, 1945. Zacks, L.: Coronary Sclerosis and Myocardial Infarction in Youth, Am. Heart. J. **26**: 269, 1944. Boas and Aldersberg.[11b]

"fluid was found in the pleural cavities but the lungs were normal. . . . The pulmonic valves showed some yellowish raised areas. The intima of the aorta contained roughened elevations which sometimes, because of their yellowish white color, resembled xanthomas. They were most pronounced in the region of the insertion of the ductus arteriosus, and here the stenosis of the aorta was most decided. The left carotid artery was nearly closed as the result of similar proliferation of the intima. The mitral valve showed four lentil-sized, yellow xanthomatous plaques. These caused distortion of the cusps and made tight closure of the valve impossible. Lesions of pinhead size were found in both coronary arteries. The other organs were essentially normal."

CASE 3.—A white boy 10 years of age died five minutes after boxing three rounds.[6d] He had received a number of blows to the chest and abdomen but had not been knocked down. After the fight he did not appear to be in any distress. At autopsy the descending branch of the left coronary artery was found to be occluded for a distance of 1 inch (2.54 cm.) by an organized thrombus beginning ½ inch (1.27 cm.) from the orifice. Distal to this occlusion were focal atheromatous changes. Several plaques of calcium were found between the intima and media, while the latter was disruptured and completely absent in areas.

CASE 4.[6b]—A boy 15 years of age complained of substernal distress for one month. Associated with this pain was nocturnal dyspnea. The electrocardiogram showed inversion of the T waves in leads 2 and 3. At autopsy there were numerous old scars in the left ventricle with a recent infarct in the apex and in the lower portion of the interventricular septum. The anterior descending branch of the left coronary artery was occluded. The right coronary artery showed moderate sclerosis.

CASE 5.—A white boy 15 years of age had had attacks of dyspnea and a sensation of substernal choking on exertion for three years.[6b] Two months prior to his death there occurred a severe attack of dyspnea and choking, which lasted one hour. An electrocardiogram made eight days prior to his death showed normal T waves. At autopsy the heart had a soft infarcted area 2.5 cm. in diameter in the posterior wall of the left ventricle. The coronary arteries showed moderate atheromatous degeneration with calcification.

CASE 6.—Sudden death occurred in a girl 13 years of age.[6a] There was atherosclerosis of the aorta and large arteries. The anterior descending branch of the left coronary artery was occluded. There was an infarct in the left ventricle with an aneurysmal dilatation and a recent rupture. The kidneys showed advanced arteriosclerotic disease.

CASE 7.—A boy 12 years of age died suddenly while running in the street.[6e] The heart showed no valvular changes The aorta, in the first part, showed slight atheromatous changes, and the coronaries were decidedly affected with atheromas. No further data are given on this case.

CASE 8.—A girl 12 years of age[6c] "died very suddenly. . . . No other lesion was found in the body beyond the disease of the coronary arteries."

REPORT OF CASE

J. W., a white boy 12 years of age, had been playing. After he had a sandwich at noon he returned to his play. A short time thereafter he was nauseated. The parents immediately took the child by car to the hospital, a distance of 6 miles. He remained conscious but was apprehensive during the trip. He was carried directly to an examining room, where he died a few minutes later, before he could be examined by the physician. According to the family physician, the boy always had been in good health. His tonsils had been removed three weeks previously.

Postmortem Observations.—The following pertinent observations were made at autopsy: A yellow tumor 1.5 cm. in diameter was in the subcutaneous tissue on the extensor surface of the right arm and a smaller tumor in the subcutaneous tissue of the left arm, with several similar tumors over the left elbow. One nodule 3 to 4 mm. in diameter was located on the lateral surface of the left knee. Three tumors were beneath the skin over each buttock, the largest 1.0 cm. in diameter. All these tumors were moderately firm, yellow and easily movable. In section the lipoid cells had infiltrated the corium. The number of cells varied in the different groups; some were in contact with the dermis, others extended down into the subcutaneous fat. There was no capsule, and giant cells were not found in the microscopic study. Usually the xanthomatous cells were large and of uniform size. The cytoplasm contained small globules of lipoid.

The only pathologic process of interest other than the xanthomas was found in the heart, coronaries, aorta and the major arteries leaving the arch of the aorta. The heart weighed 250 Gm. and was considered to be probably within the range of normal. The cusps of the aortic valve were fibrotic, thickened and gray (fig. 1). There was some widening at the points of their attachment. The aortic valve measured only 4 cm. in circumference, the mitral and pulmonary valves measured 7 cm. each and the tricuspid 10 cm. There were a few small yellow areas in the mitral valve. The orifice of each of the coronary arteries was decreased. The lumen of both coronaries for 2 to 3 cm. was decidedly decreased by atheromatous plaques. In fact, the lumen could not be demonstrated

Fig. 1.—The cusps of the aortic valve are thick. An atheromatous plaque involves the greater portion of the circumference of the aorta immediately above the valve. Smaller but similar plaques are present throughout the aorta and in the larger vessels arising from the arch.

grossly in the first portion of the anterior descending branch of the left coronary artery. The amount of lipoid material decreased in these vessels after the first 2 to 3 cm. The myocardium showed extensive parenchymatous degeneration, but definite areas of infarction were not demonstrated.

In the aorta above the aortic ring was a large plaque which extended up for 2.5 cm. and almost completely encircled the lumen (fig. 1). Smaller but similar plaques were distributed throughout the entire length of the aorta. They were more numerous in the lower third. The innominate, left carotid and left subclavian arteries had plaques similar to those in the aorta. Approximately one half of the circumference of the lumen of the innominate artery was a solid mass of yellow material.

The histologic lesions were similar in each of these large arteries. It would appear wise, however, to discuss separately the changes observed in each of the three parts of the wall of these arteries. In those portions of the intima that were yellow without plaque formation large lipoid cells infiltrated the

tissue. In the plaques lipoid cells were numerous, with cholesterol crystals in moderate numbers and focal areas of polymorphonuclear leukocytic infiltration. There were some cystic areas of degeneration in these plaques. The outer surface usually stained pink with phloxine ad hematoxylin. Few spindle-shaped cells were present, giving the area a suggestion of fibrous-like tissue. Calcium was not observed in any of the plaques. The lumens of the coronary arteries were not completely occluded but decidedly decreased (fig. 2).

The changes in the tunica media varied in different portions of the vessels (fig. 3). In those areas where the intima was infiltrated with few lipoid cells, the media was normal. However, in the aorta where the plaques were located the media was infiltrated by many lipoid cells. These cells frequently were continuous with those in the overlying plaque. In other areas the lipoid cells were in small groups, sometimes around the vasa vasorum (fig. 3 *D*). The elastic fibers were completely absent in the areas occupied by the lipoid cells (fig. 3 *C*). These elastic fibers apparently were degenerated and broken in these local areas. Sometimes a few lipoid cells separated the bands of elastic tissue. In other areas of the media, beneath the intimal plaques, the elastic fibers were swollen and stained deeply with phloxine. The number of nuclei in such areas, which appeared to be undergoing degeneration, was definitely decreased. The media, distal to the already described foci of degeneration, was diffusely infiltrated with polymorphonuclear leukocytes (fig. 3 *B*). There seemed to be an increase in the amount of pink-staining ground substance separating the bundles of elastic tissue. In some areas of the coronaries, the media was swollen and the elastic fibers were fragmented.

The adventitia in the aorta appeared to be thicker than normal. Collections of lymphocytes were numerous in some areas (fig. 3 *A*). Smaller numbers of similar cells were present in the adventitia of the coronaries. The walls of the vasa vasorum were thick and their lumen decreased. However, no specific pathologic change was recognized except for occasional perivascular lymphocytes.

There were a few petechiae in the lungs and a small amount of pulmonary edema. The spleen weighed 275 Gm.; but pathologic changes were not observed. The reticuloendothelial system, as found in the spleen, liver, bone marrow and lymph nodes, was carefully studied, but significant lesions were not found. There was some proliferation of the reticuloendothelial cells in the sinuses of some of the lymph nodes; however, there was nothing to suggest such processes as one finds in lipoid dystrophies.

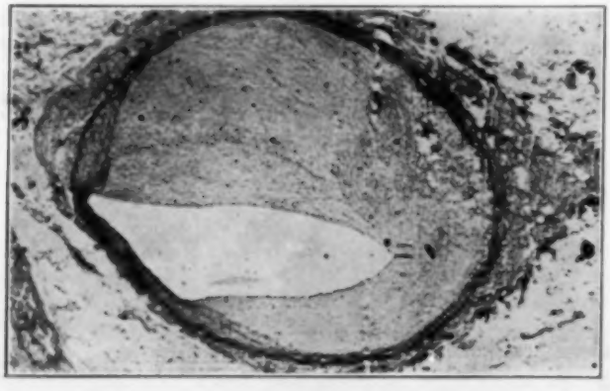

Fig. 2.—The lumen of the descending branch of the left coronary artery is decreased. Death of this boy 12 years of age is considered to have resulted from coronary insufficiency (Verhoeff-Van Gieson stain, × 26).

Anatomic Diagnosis.—The following conditions were observed: multiple xanthomas in subcutaneous tissue of the arms, around the elbows, knees and buttocks; cholesterol plaques in the aorta and coronary, innominate and subclavian arteries; aortic stenosis, cholesterol plaques in mitral valve; decided decrease in the lumen of the anterior descending branch of the left coronary artery; degeneration of the media of the aorta and coronaries wtih an infiltration of lipoid cells; polymorphonuclear leukocytes in the media of the aorta; parenchymatous degeneration of the myocardium; petechiae in the lungs, and pulmonary edema.

COMMENT

The clinical and pathologic data are incomplete in some of the reported cases of xanthomas and arteriosclerosis in children 16 years of age or younger. However, it would appear from the available information that the cardiovascular lesions are similar in all cases, whether or not xanthomas are present. In each of these cases in which cholesterol determinations were made, the amount was found to be increased. It has been stated that in all cases of xanthoma tuberosum there is hypercholesteremia.[10] In many of the cases with arteriosclerosis, death occurred without laboratory studies having been made. In some of the cases there were no prodromal signs or symptoms of heart disease.

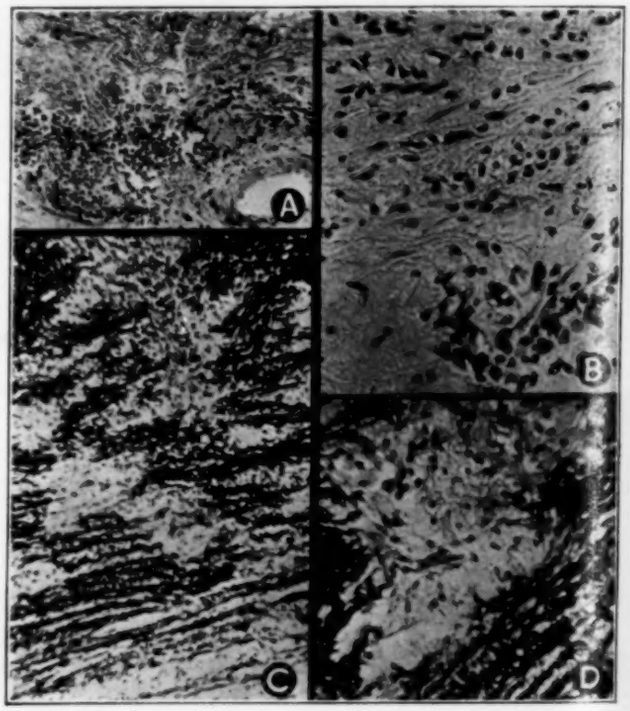

Fig. 3.—Photomicrographs, slightly reduced from the magnifications indicated: *A*, the adventitia of the aorta is thickened, and in some areas there are groups of lymphocytes about the vasa vasorum (hematoxylin and phloxine, × 275); *B*, the media beneath the large intimal plaque frequently is infiltrated with polymorphonuclear leukocytes. Note the collection of these cells around a small vessel (hematoxylin and phloxine, × 275); *C*, the elastic fibers in the media have degenerated in many focal areas. These foci are infiltrated with lipoid cells (Verhoeff-Van Gieson stain, × 108); *D*, lipoid cells are present in the plaques and infiltrate the media (Verhoeff-Van Gieson stain, × 120).

The immediate cause of death in this group of cases usually was occlusion of the anterior descending branch of the left coronary artery. In this group of 24 cases there were 14 females and 10 males. All the cases occurred in white patients. There are too few cases for these data to be significant; however, they are of interest.

The atheromatous plaques in the case reported herein are interesting when compared with the experimental lesions reported by Cowdry [16] in the rabbit. In this human case the atheromatous lesions were present in the first and lower third of the aorta; the development of the plaques would seem to agree with the

16. Cowdry, E. V.: Arteriosclerosis, New York, The Macmillan Company, 1933.

theory advanced for this lesion in the rabbit. Apparently the pathologic changes in the media are more pronounced in children than in the experimental animal. Jokl and Greenstein [6d] referred to the media in their case as disrupted and completely absent in areas. In our case the elastic tissue in the media usually was fragmented and sometimes completely absent in focal areas beneath the intimal plaques. From casual observation the media has the appearance of a syphilitic lesion, as do the groups of lymphocytes around the vasa vasorum in the adventitia. Hess [8a] also referred to the similarity of these changes in the aorta to syphilitic aortitis in a case of xanthoma tuberosum and arteriosclerosis in a girl 19 years of age.

It is impossible to say why xanthomas and sclerotic plaques developed in our case, but the pathologic change appears to have occurred as follows: The lipoid cells first appeared in the intima, probably in the largest numbers at the junction of the intima with the media. The number of these cells increased to form the intimal plaques. Degeneration and fibrous proliferation occurred within the plaques. The media beneath these plaques degenerated, as shown by the variation in staining of the elastic fibers, their swelling and the infiltration of polymorphonuclear leukocytes between the elastic fibers. The occurrence of the degeneration beneath the plaques may support the idea that the nutrition for the media comes from the blood in the lumen of the vessels.[16] The presence of these large intimal plaques would either decrease or prevent any nutrition from the circulation reaching the media through the intima. Medial degeneration frequently occurs in human cases of arteriosclerosis; however, the extensive fragmentation of the elastic fibers and the large numbers of lipoid cells have not been observed in adult cases in such proportions as in this boy aged 12 years. The swelling of the media and the fragmentation of the elastic fibers in the localized areas of the coronary artery would suggest that some degenerative change occurred in the elastic tissue before the areas were infiltrated with lipoid and inflammatory cells. Although calcium was not present in our case, it has been observed by others in the sclerotic plaques in children.[17] A more careful study of the cases of arteriosclerosis that occur in children may contribute greatly to a better understanding of the process of arteriosclerosis in adults.

SUMMARY

A case is reported of sudden death in a boy 12 years of age who had xanthoma tuberosum and arteriosclerosis with a decided decrease in the size of the lumen of the anterior descending branch of the left coronary artery. Twenty-four cases of sudden cardiac death now have been reported in children 16 years of age or younger at the time of the onset of cardiac symptoms in whom arteriosclerosis was present. Xanthomas were present in 18 of these cases. The most frequent cause of death in the group was coronary occlusion.

The pathologic changes occurring in this case are reported in detail. There were atheromatous plaques in the aorta and in the coronary, carotid, innominate and subclavian arteries. Extensive degenerative changes were observed in the media of the aorta, and collections of lymphocytes were present in the adventitia of this vessel.

17. Cook, Smith, Giesen and Berdez.[2] Sprague and Orgain.[6b] Jokl and Greenstein.[6d]

EFFECTS OF PITUITARY ADRENOCORTICOTROPIC HORMONE (ACTH) THERAPY IN OPHTHALMOLOGIC CONDITIONS

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The demonstration of the dramatic effects induced in patients with rheumatoid arthritis with the use of certain products of the adrenal cortex and the pituitary adrenocorticotropic hormone (ACTH) by Hench and his co-workers [1] has been followed by the demonstration of the therapeutic value of these products in a wide variety of disease conditions. In most instances the therapeutic value ceases with or shortly after the cessation of treatment.[2] Nevertheless, the implications and potentialities of this and related treatment are fraught with significance. It was only natural that we should investigate the use of these substances (in this instance only pituitary adrenocorticotropic hormone to date) in ophthalmology. The known effect of these products on the acute inflammatory diseases of structures composed of collagenous tissue [2] and of mesenchymal tissue rendered the eye a suitable organ for experimental treatment because the sclera and cornea contain such a high collagen content and because the uveal tract is the seat of so much disease. The claims of Mousio-Fournier [3] in the Fournier treatment of retinitis pigmentosa with the use of the melanophore hormone suggested the use of pituitary adrenocorticotropic compound in this condition because the compound contains a high content of melanophore hormone as an impurity. It is of significance that Vail [4] prophesied the experimental use of pituitary adrenocorticotropic hormone in the treatment of certain hopeless eye conditions, specifically retinitis pigmentosa, in a recent editorial.

Pituitary adrenocorticotropic hormone was administered to 6 patients with the following diseases: severe corneal edema (keratitis bullosa) due to an underlying corneal dystrophy, secondary glaucoma, chronic iridocyclitis, retinitis pigmentosa and acute choroiditis. The duration of treatment was controlled by the short supply of the medicament and the response of the patient. Treatment was discontinued after twelve hours in 1 patient because it was feared that longer treatment without surgical intervention would jeopardize the patient's eye. In no instance was treatment continued longer than nine days, 1 patient receiving the drug four days, 2 nine days, 1 six days and 1 twelve hours.

Pituitary adrenocorticotropic hormone was supplied by Dr. John R. Mote of Armour and Company.

Read before the Association for Research in Ophthalmology, Eastern Regional Meeting, Jan. 28, 1950.

From the Department of Surgery (Ophthalmology), the New York Hospital-Cornell University Medical Center.

Drs. Ephraim Shorr, May G. Wilson, Katherine Hain and Anne C. Carter gave assistance and advice in this study.

1. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: The Effects of the Adrenal Cortex (17-Hydroxy-11-Dehydrocorticosterone (Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis: Preliminary Report, Proc. Staff Meet., Mayo Clin. **24**: 181, 1949. Hench, P. S.; Slocumb, C. H.; Barnes, A. R.; Smith, H. L.; Polley, H. F., and Kendall, E. C.: The Effects of the Adrenal Cortical Hormone 17-Hydroxy-11-Dehydrocorticosterone (Compound E) on the Acute Phase of Rheumatic Fever: Preliminary Report, ibid. **24**: 277, 1949.

2. Panel Discussion on Present Status of Cortisone and ACTH, Medical Education Committee, New York Academy of Medicine, Jan. 12, 1950.

3. Mousio-Fournier, J. C.: Therapeutic Action of Pituitary Extract on Diverse Eye Affections, Dia. méd. urug. **16**: 317, 1949.

4. Vail, D.: ACTH in Myasthenia Gravis, Am. J. Ophth. **32**: 1414, 1949.

Metabolic studies were instituted prior to treatment in all cases but one (secondary glaucoma) and during and after the treatment as indicated, in an attempt to evaluate the fact that the adrenal cortex was being stimulated and to determine the degree of that stimulation. We were interested in determining whether a complete adrenal cortical response was necessary to secure good local (ocular) therapeusis. If a good therapeutic response could be secured on small dosages, treatment could be continued over a longer period without the risk of adverse systemic complications. As the circulating eosinophil count offers a good index of the pituitary adrenocorticotropic hormone dosage and maintenance dosages, these figures are given with the case histories.

REPORT OF CASES

CASE 1.—*Corneal Edema (Corneal Dystrophy).*—S. G., a white man aged 46, lost his right eye in 1921 after a postoperative infection. He had a lens extraction of the left eye in 1926, which gave him a corrected vision of 20/20. In 1945 blurred vision developed, and he was examined by several ophthalmologists who told him that he had glaucoma. He was placed on a therapeutic regimen of pilocarpine nitrate and physostigmine salicylate eye drops. He was later informed that

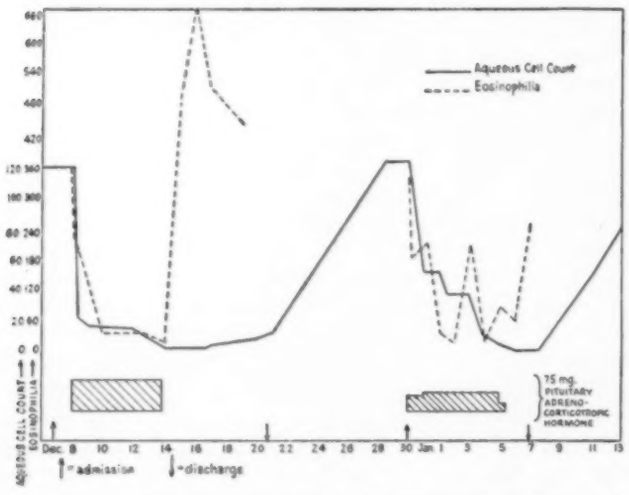
Aqueous Cell Count
Eosinophilia
75 mg. PITUITARY ADRENO-CORTICOTROPIC HORMONE
Dec. 8 10 12 14 16 18 20 22 24 26 28 30 Jan 1 3 5 7 9 11 13
↑-admission
↓-discharge

Fig. 1 (case 3).—Apparent relation of improvement to decrease in eosinophilia: the broken line represents eosinophilia, the straight line indicates the number of cells in the aqueous of the left (poorer) eye.

he did not have glaucoma but rather had a corneal dystrophy with edema. He was told to continue the use of pilocarpine eyedrops and to use dextrose and karo® topically.

When he was examined at the New York Hospital on July 20, 1949 he was found to have surgical anophthalmos on the right and vision of $20/70 + 2$ with glasses on the left. His cornea was decidedly edematous, with an irregular surface and pronounced thickening. There were several large subepithelial blebs. There were some secondary remnants in the pupillary area. Tension was 20 mm. of mercury with the Schiötz tonometer.

He was admitted for treatment with pituitary adrenocorticotropic hormone on Dec. 7, 1949 and given 25 mg. four times daily, for a total of sixteen injections. There was no apparent improvement in vision or in the appearance of the cornea after this interval, nor was there any adverse change in his ocular or systemic condition.

His circulating eosinophil count was 374 per cubic millimeter on admission, dropping to 171 four hours after the first injection of the drug. It measured 2 per cubic centimeter on the second day of therapy, 6 on the third day and 86 on the fourth day.

CASE 2.—*Secondary Glaucoma.*—I. W., a white man aged 62, was seen in the Eye Clinic of the New York Hospital in 1935 with a visual acuity of 20/20 and 20/15. He returned in 1949 with bilateral cataracts. On Aug. 10, 1949 he had an uneventful iridotomy and intracapsular lens extraction on the right followed by a similar procedure on the left on Aug. 16, 1949. While in the hospital he exhibited no untoward local reaction. His pupils never dilated well with the local atropine instillations. Two weeks after the first operation a faint

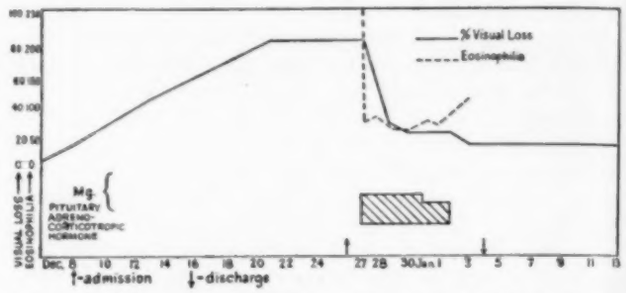
% Visual Loss
Eosinophilia
Mg. PITUITARY ADRENO-CORTICOTROPIC HORMONE
Dec. 8 10 12 14 16 18 20 22 24 27 28 30 Jan 1 3 5 7 9 11 13
↑-admission
↓-discharge

Fig. 2 (case 5).—Apparent relation of improvement in vision to decrease in eosinophilia. Broken line represents number of circulating eosinophils, straight line represents percentage of visual loss, using the American Medical Association tables for computation of visual acuity loss in percentages.

aqueous ray and a few cells were noted in the right eye, followed by the appearance of an early inflammatory membrane in the pupillary area. One week later a similar event was noted in the left eye. The intraocular tension of the two eyes was within normal limits. On Nov. 8, 1949 the tension of the right eye was 48 mm., and of the left 26 mm. (Schiötz). He was admitted to the hospital, where a synechiotomy and discission of the membrane was performed on the right eye. The next day his eyeball was hard and the cornea steamy. A paracentesis afforded some relief.

On November 16 a basal iridectomy was performed on the right eye, following which the tension remained within normal limits. He was discharged on November 21. He returned on December 13 with a painful, red right eye and tension 65 mm. (Schiötz). He was admitted to the hospital for a short trial period of pituitary adrenocorticotropic hormone therapy of twelve hours. Four hours after the first injection his tension had dropped to between 35 and 38 mm. (Schiötz). However, within eight hours it again rose to its former level; treatment was discontinued and surgical intervention performed.

His eosinophil count on admission was 92 per cubic millimeter; it fell to 25 four hours after the first injection and reached zero twelve hours after the first injection. There were no other observations which were relevant to the use of pitui-

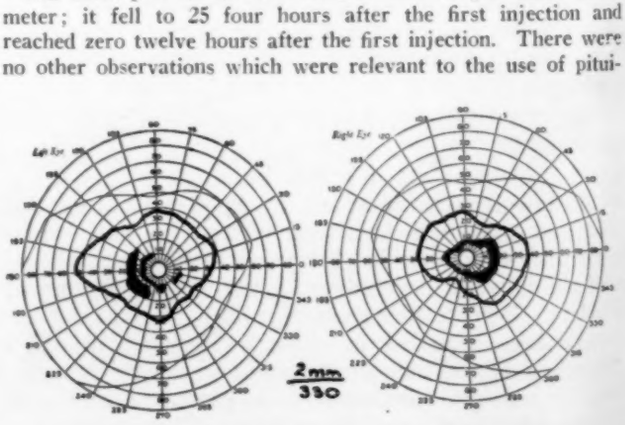

Fig. 3 (case 4).—Visual fields Dec. 15, 1949 before treatment.

tary adrenocorticotropic hormone. He received a total of 75 mg. of the hormone before surgical intervention.

CASE 3.—*Chronic Iridocyclitis.*—J. K., a white boy aged 9, was referred to the Eye Clinic of the New York Hospital from Tilton General Hospital on May 18, 1948. There was a history of blurring of vision in both eyes since the summer of 1947. He was first seen on Dec. 4, 1947, at Tilton, where a bilateral iridocyclitis with vitreous membranes was found. "Laboratory studies during this hospitalization showed the

blood cell count, reaction of the blood to the Kahn test and sedimentation rate to be within normal limits. A roentgenogram of the chest revealed the presence of healed tubercular thoracic lymph nodes. Reaction to the brucellosis skin test was 1 plus after forty-eight hours. Response to the old tuberculin test was 1 plus after twenty-four and forty-eight hours with a dilution at the strength of 1 : 1,000." [5] He was given a course of penicillin with a total of 1,050,000 units and a six week course of streptomycin with a total of 12 Gm. In addition, he was using atropine instillations. "No definite focus of infection was ever established." [5] He was given a course of desensitization to old tuberculin in the Allergy Clinic at Tilton General Hospital. The visual acuity was 20/70 for each eye before and after hospitalization. The working impression was: "cyclitis, chronic, plastic, bilateral, cause undetermined, associated with fibrous bands in both vitreous bodies, vision 20/70 each eye uncorrectible." [5]

The patient has been followed in the Eye Clinic of the New York Hospital from May 18, 1948 to the present. Thorough examinations have failed to give any clue as to the cause of his uveitis. The roentgenology department reported that roentgenograms of his chest revealed essentially normal conditions. During this entire period he has been receiving atropine instillations constantly with the exception of a few days. Attempts to stop the use of atropine are immediately followed by symptoms of irritation of the ciliary body. The nearest to a free interval which he has enjoyed was March 12 to May 7,

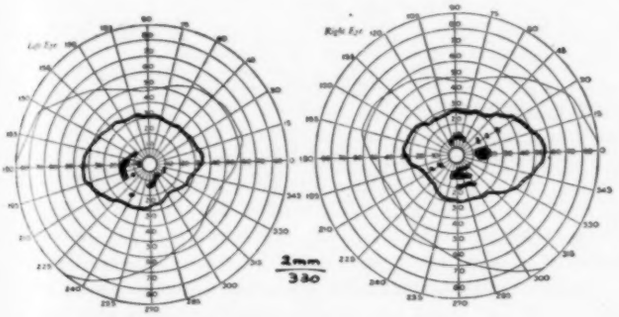

Fig. 4 (case 4).—Visual fields December 22 on fifth day of treatment. Note marked decrease in density of ring scotomas.

1949, when he was practically free of aqueous ray and cells, with faint ray and "few cells" reported occasionally during this period. His vision has slowly improved to between 20/40 to 20/30— corrected in each eye. He is somewhat noncooperative; as a result, precise visual acuity recordings are difficult.

He was admitted to the hospital on Dec. 7, 1949 for treatment with pituitary adrenocorticotropic hormone. At that time he had a 2 plus beam on the right and 3 plus on the left, with over a hundred cells in each narrowed beam field on slit lamp examination. There were fine keratic precipitates on each cornea, dense synechiae at 6 o'clock in each eye and extensive vitreous membranes. Vision on admission was 20/40 — 3 right and 20/30 — 3 left. The instillation of atropine was discontinued at the time of admission.

Treatment with the adrenocortical agent was started on December 8 and stopped December 14. He was given 25 mg. three times daily, for a total of twenty-one injections (525 mg.). Within nine hours of the first injection definite improvement was noted, with plus-minus beam in the right eye, 1 plus beam in the left and a few cells in each. From then until December 12 he exhibited plus-minus beam in each eye with 3 to 5 cells on the right and 10 to 15 on the left, in the whole anterior chamber. By December 14, he was completely free of aqueous beam and no cells were found in either anterior chamber. His vision was 20/30 — 1 right and 20/30 — 2 left. It was our impression that the vitreous membranes had decreased in density. This is difficult to evaluate. There was no change observed in the density of the synechiae.

5. From a letter sent by the Eye Service of the Tilton General Hospital on May 21, 1948.

Three days after cessation of treatment there was a plus-minus beam in each eye with 1 to 2 cells on the right and 3 to 5 on the left. This state continued until Dec. 21, 1949, when he had a 1 plus aqueous ray in each anterior chamber, with 4 to 5 cells in the narrow beam on the right and 12 to 15 on the left. He was discharged at this point. He returned to the clinic on December 27 with a 2 plus beam on the right, 3 plus

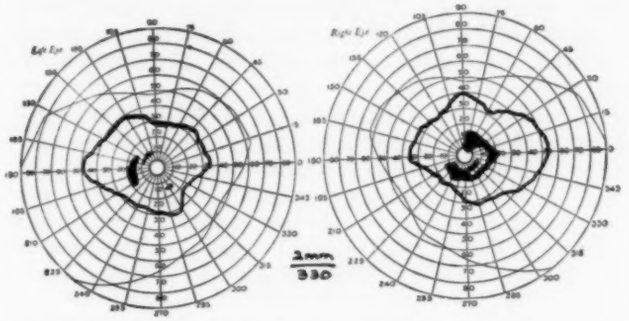

Fig. 5 (case 4).—Visual fields December 27, the day after cessation of treatment.

on the left and well over 100 cells in the narrow beam in each eye. On December 30 the observations were the same, with vision as of December 27, right 20/30 — 2, left 20/40. Instillations of atropine had been started on December 27. He was readmitted to the hospital on December 30, at which time the atropine was discontinued.

On his first admission his circulating eosinophils totaled 349 per cubic millimeter. Four hours after the first injection they dropped to 208. On December 9 they totaled 135, with 31 on December 12 and on December 13. On December 14, the last day of treatment, they totaled 12. They had risen to 496 by the next day, 661 by December 16, 515 by December 17 and 435 by December 19. No other significant laboratory data and no significant physical changes, other than those reported in the eyes, were noted during his stay in the hospital or on his return to the clinics.

He was readmitted to the hospital on Dec. 30, 1949; he received 12.5 mg. of pituitary adrenocorticotropic hormone four times daily until Jan. 6, 1950, for a total dosage of 300 mg. He had a 2 plus aqueous beam on the right and 3 plus on the left, with over 100 cells in each narrow beam field on slit lamp examination; on December 31, 2 plus beam right with 15 to 20 cells, 2 plus beam left with 40 to 50 cells, and on Jan. 1, 1950 plus-minus beam on the right with about 25 cells and

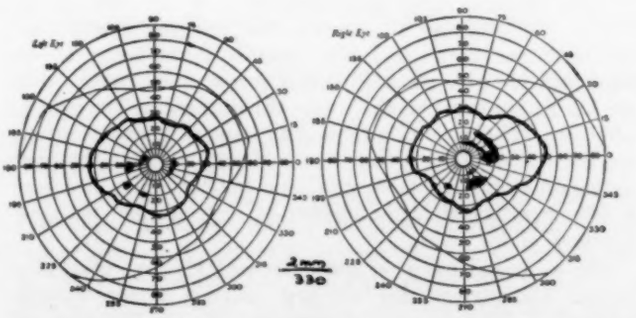

Fig. 6 (case 4).—Visual fields Jan. 4, 1950, nine days after cessation of treatment.

1 plus beam on the left with about 50 cells. The next day he had a plus-minus beam with 7 to 10 cells right and 1 plus beam with 25 cells left. On January 3 he had 1 plus beam right with 15 to 20 cells, 2 plus left with 25 cells; on January 4, plus-minus beam right with 2 to 5 cells and 1 plus beam left with 10 to 15 cells; on January 5, faintest beam in each eye, with 5 cells right and 1 to 2 left, and on January 6 he was symptom free.

Case 4.—*Retinitis Pigmentosa.*—H. S., a white man aged 25, had had nightblindness since 1943. The patient had typical early retinitis pigmentosa. He has been treated over a period of four years with various medicaments, including cod liver oil injections, vitamin A, nicotinic acid and alpha-tocopherol, without improvement. He was admitted to the New York Hospital on December 15 for treatment with pituitary adrenocorticotropic hormone. Vision on admission was 20/50 + 2 on the right (missing 2 in 20/50 line) and 20/30 — 3 left (missing 2 in 20/40 line). He was started on the drug, 25 mg. four times daily, on Dec. 17, 1949 and received treatment for nine days.

On December 19 he was able to see two letters in the 20/30 line with the right eye and two letters in the 20/20 line with the left eye. On December 21 vision was 20/30 + 2 with each eye. The next day, although he was able to identify only two letters in the 20/30 line, he was able to identify two symbols in the 20/20 line. From then until cessation of treatment on December 26 vision was 20/30 — 3 right and 20/30 + 3 left. At the time of discharge on December 28 he read 20/40 + 1 right (missing 3 in 20/40 line) and 20/30 + 1 left (missing 3 in the 20/30 line). His near vision at all times was such that he could read Jaeger type 1. Unfortunately, some abdominal distress developed during the last several days of his hospitalization, persisting until three days after discharge, and he believed that this interfered with his vision.

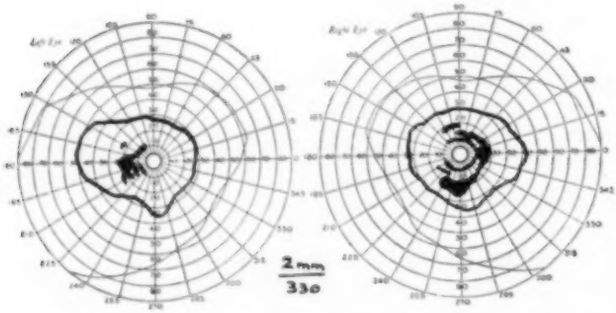

Fig. 7 (case 4).—Visual fields January 11, sixteen days after cessation of treatment: the ring scotomas are becoming quite dense.

His visual fields were interesting. He had a complete ring scotoma on the right and incomplete double ring on the left at the time of admission. On December 22, five days after institution of treatment, he showed an increase in the right peripheral field of about 15 degrees temporally with a decrease of 10 degrees in the left temporal and 18 in the left superior field. However, the ring scotomas were definitely broken up, as noted on the charts. On December 27, one day after cessation of treatment, the right peripheral field was essentially the same as on December 22, with about 10 degree increase superiorly, while the left peripheral field was larger although not as large as on admission. The right field showed an incomplete ring scotoma; the left was much as it had been on December 22. The same technician plotted all three fields and felt that there had been a definite reduction in the number of scotomas and the completeness of the rings.

The eosinophil count on admission was 325 per cubic millimeter. Four hours after the first injection of the hormone on Dec. 17, 1949 the count dropped to 153. On December 19, 20, 21, 22, 23, 25, 27 and 28 it was 6, 12, 6, 3, 17, 6, 447 and 478, respectively. Treatment had been stopped on December 25. On December 20 he had a 1 plus reaction for sugar in his urine; on December 22 he had a fasting blood sugar level of 101 mg. per hundred cubic centimeters. The urine was free of sugar in measurable quantities at all other times. His blood pressure on admission was 150 systolic and 80 diastolic. It was considered that this elevation was due to the excitement attendant on hospitalization. The blood pressure reached 166 systolic and 90 diastolic on December 25 and fell to 132 systolic and 70 diastolic the next day. There were no other significant physical or laboratory alterations observed, other than those noted in the eye examinations.

In December, after his discharge from the hospital, his vision was right 20/30 + 3 and left 20/30 + 3. On January 4, 1950 it was 20/30 + 1 and 20/30 + 3. The two visual field studies made on these dates indicate a progressive increase in the thickness of his ring scotomas, approaching the pretreatment picture.[5a]

Case 5.—*Acute Choroiditis.*—V. G., a white woman aged 31, a physician, in 1944 had noted halos in front of the left eye for a period of about three months. She was examined by a physician then, although no definite diagnosis was made. In October 1949 the symptoms recurred with increased severity. At that time evidence of choroiditis was noted in the upper temporal quadrant. The vitreous was full of inflammatory products. She was seen in consultation by one of us (J. M. M.) on Nov. 22, 1949, at which time her vision was right 20/20— and left 20/40. The tensions were within normal limits. There were numerous cells in the aqueous with severe inflammatory reaction in the vitreous on the left and with two large areas of choroiditis seen hazily in the superior temporal quadrant. No clues had been found as to the etiologic agent.

Her condition became worse in spite of atropine given locally, penicillin injections, removal of a tooth and oral use of aureomycin. She was admitted to the New York Hospital on Dec. 26, 1949. By this time her vision on the left was 20/200; there were a few cells in the anterior chamber, 1 plus aqueous ray and the vitreous so full of inflammatory products that the areas of choroiditis could barely be discerned.

On December 28 she was given an initial dose of 50 mg. of pituitary adrenocorticotropic hormone followed by a 25 mg. dose four times daily. This was reduced to 25 mg. three times daily on December 31 and stopped on Jan. 1, 1950. The total dose was 550 mg. One day after beginning the hormonal therapy her vision on the left was 20/50 — 2 and the vitreous had begun to clear slightly. On Dec. 30, 1949 vision on the left was 20/40 — 4 and on December 31, 20/50 + 2. Occasionally her vision was slightly better as the eye would "seem to clear." On Jan. 1, 1950 her vision was 20/30 — 3; the vitreous was slowly clearing and vague fundus detail was becoming visible. Her vision on discharge January 4 was 20/40 — 3 + 2. The vitreous still contained considerable exudate, although much less than at the time of admission. There were no cells noted in the anterior chamber, nor was there an aqueous ray.

Her circulating eosinophils were 245 per cubic millimeter on admission; the value fell to 68 four hours after an initial dose of 50 mg. of pituitary adrenocorticotropic hormone on Dec. 27, 1949. On December 28, 29, 30 and 31 it was 74, 6, 6 and 20, respectively; on Jan. 1 and 2, 1950 it was 12 and 107, respectively.

Case 6.—*Acute Choroiditis.*—N. W., a white man aged 38, was admitted to the New York Hospital on Jan. 6, 1950 with acute choroiditis of the left eye, of two days' duration. Although this case is incomplete, it is believed that the points to be learned from it are sufficiently important to warrant its inclusion. On admission his vision was 20/20 on the right and 20/200 on the left. The ocular lesion consisted of an acute focus of choroiditis underlying a vessel above the macula, with edema of the macula and lower pole of the disk, extending into the inferior retina. Vitreous cells were not observed.

Pituitary adrenocorticotropic hormone therapy, 25 mg. every six hours, was started on January 7. On January 8 there was a slight increase in edema; by the morning of January 9 it had increased so that the disk was seen hazily because of the edema at both inferior and superior poles. The macular edema had also increased. At this point we considered stopping treatment with the drug. However, eight hours later on the same day the edema had receded noticeably and vision was

5a. Twelve weeks after cessation of treatment this patient's regression had not reached the pretreatment level.

20/200 + 1. His vision was 20/100 the morning of January 10 and by late afternoon was a poor 20/70. The edema was receding slowly, although the disk area was still edematous. On January 11 the lesion was definitely smaller and less blurred in appearance. His vision was 20/70 + 2. The next day he was able to read a poor 20/40 and with a + 3.00 D. lens (since he was completely atropinized) he could read Jaeger type 7 slowly. The lesion above the macula was now beginning to assume a fragmented appearance. On January 13 he was able to read 20/40— and with a + 3.00 D. lens could read Jaeger type 3 slowly. On January 14 he was able to see 20/40 + 2. The lesion appeared more fragmented and the macular area less edematous. The center of the lesion exhibited faint pigmentation. By January 17 he was able to read 20/30 + 2 with the eye which was completely atropinized and with a + 3.00 D. lens could read Jaeger type 1. There was still considerable edema about the disk, though less than during the first days. The lesion was less fluffy (less edematous), with central pigmentation increasing. No vitreous cells were found.

He had eosinopenia (74 eosinophils per cubic millimeter) on admission. His blood pressure was 160 systolic and 104 diastolic on admission; it rose to 196 systolic and 100 diastolic during the first several days, after which it dropped to near its original figure. This will be discussed in a later paper.

ANALYSIS OF RESULTS

The most dramatic responses to pituitary adrenocorticotropic hormone were made by the patients with uveitis (anterior and posterior). The recurrence of symptoms after discontinuation of the drug in the child with uveitis, the complete therapeutic response on resumption of treatment and this in turn followed by recurrence after cessation of the second series of treatments parallel the experiences of workers in the field of rheumatoid arthritis and other conditions. The patient with the posterior uveitis (choroiditis) has continued to improve although treatment with the drug has been discontinued (case 5).[5b]

The different courses taken by the two forms of uveitis treated (acute choroiditis and chronic iridocyclitis) are not paradoxic; rather, they are the expressions of an acute process contrasted to those of a chronic recurrent process. One would expect acute choroiditis to continue healing, once well started in that direction, just as one would anticipate recurrences in chronic iridocyclitis. In case 3 the child with chronic iridocyclitis was given 525 mg. of pituitary adrenocorticotropic hormone before he secured a complete therapeutic response on his first admission and 300 mg. of the drug to secure the same result on the second admission. Three theories suggest themselves; his daily dosage was unnecessarily high during his first admission, the first series conditioned him to a better response during the second series or the observations were simply coincidental.

The response of the patient with retinitis pigmentosa (case 4) is more difficult to evaluate. This is a hopeless condition, unaccompanied with remissions, and the patient is an excellent observer. It was our feeling that he did gain an increase in visual acuity and a decrease in density of his ring scotomas. The decrease in the size of his left peripheral field following the initial treatment is one of the paradoxes which investigators constantly encounter, to their embarrassment, and which they are not able to explain on all occasions. The fact that his ring scotomas became denser after the treatment was discontinued would indicate that he did have a temporary improvement. Again, the recurrence following cessation of treatment is what one might expect in a chronic disease. It is paradoxic that retinitis pigmentosa should be benefited by pituitary adrenocorticotropic hormone. Hench and his co-workers noted that patients with rheumatoid arthritis were benefited by pregnancy; hence, the energies of these investigators were stimulated toward research which has culminated in cortisone and pituitary adrenocorticotropic hormone. One of us (D. M. G.), who conducts the retinitis pigmentosa clinic of the New York Hospital, has consistently noted that patients with retinitis pigmentosa complain of an increase in the severity of their disease with each successive pregnancy.

The failure of treatment in the patients with the corneal edema (case 1) and the secondary glaucoma (case 2) cannot be productive of any conclusions as to the efficacy of the drug in these conditions. The duration of treatment was too short and the series of cases far too small to permit any pertinent conclusions.

The response of the patient with the acute choroiditis near the macula (case 6) was most unusual, in that he failed to throw any inflammatory products into the vitreous, suffered a decided initial increase in retinal edema coincident with the onset of treatment, improved rapidly coincident with the early phase of his treatment and began his healing in an unorthodox manner. Characteristically, an area of choroiditis will shrink as it begins to heal. In his case the lesion began to fragment and show areas of clearing as recovery ensued.

COMMENT AND SUMMARY

1. Pituitary adrenocorticotropic hormone (ACTH) was given to 6 patients with the following diseases: severe corneal edema (corneal dystrophy), secondary glaucoma, chronic iridocyclitis, retinitis pigmentosa and acute choroiditis. The response of the patients with iridocyclitis and choroiditis was dramatic, that of the patient with retinitis pigmentosa apparently temporarily beneficial. The other 2 patients failed to exhibit any favorable response to short courses of treatment. No adverse systemic effects were noted other than temporary hypertension and glycosuria (1 plus) and mild abdominal distention in 1 patient and temporary hypertension in another.[6]

2. Every patient showed a definite fall in circulating eosinophils, similarly shown by Thorn, Forsham, Prunty and Hills.[7] Two patients (cases 2 and 6) had eosinopenia on admission.

3. The suggestion is offered that pituitary adrenocorticotropic hormone may function to condition otherwise refractory patients to an excellent therapeutic response to some other subsequent treatment which is insufficient, in itself, to secure such a result, e. g., fever therapy in uveitis. It may also serve to break up a vicious cycle of events, such as secondary glaucoma complicating uveitis. These speculations remain to be proved.

5b. Ten weeks after cessation of treatment visual acuity of this patient has remained 20/30, and there has been no inflammatory release.

6. Both these patients received pituitary adrenocorticotropic hormone from a lot which contained 0.2 unit oxytocin and 1.3 unit vasopressin.

7. Thorn, G. W.; Forsham, P. H.; Prunty, F. T. G., and Hills, A. G.: A Test of Adrenal Cortical Insufficiency; The Response of Pituitary Adrenocorticotropic Hormone, J. A. M. A. **137**: 1005 (July 17) 1948. Forsham, P. H.; Thorn, G. W.; Prunty, F. T. G., and Hills, A. G.: Clinical Studies with Pituitary Adrenocorticotropic Hormone, J. Endocrinol. **8**: 15, 1948.

4. The short supply of pituitary adrenocorticotropic hormone and cortisone militate against the study of any large series of cases at the present time.

5. The instructional value of this material plus the fact that this represents the first report on the use of the drug in ophthalmologic conditions warrants this preliminary report, although the series is far too small to permit any conclusions. Further investigation is definitely indicated and is being prosecuted.

EFFECT OF ACTH ON CERTAIN INFLAMMATORY DISEASES OF THE EYE

A Preliminary Report

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The current investigation, with which this preliminary report is concerned in part, was motivated by several considerations. First, artificially induced fever used in the treatment of many of the inflammatory disorders of the eye frequently may achieve the desired effect by the acceleration of the mechanisms normally evoked in many stress states. In this regard, the results of recent laboratory and clinical research are such as to ascribe a basic role to the adrenal gland. Second, the eye is particularly suited, as is no other organ, for direct and minute visualization of disease processes. Here the vascular, cellular and exudative changes of both primary and secondary disease can be observed. In a sense, this opportunity may be considered comparable to that which Markee [1] recognized when he visualized the hormonal response of endometrial tissue implanted in the anterior chamber of the monkey's eye. Thus, to be able to directly observe the action, if any, of pituitary adrenocorticotropic hormone (ACTH)[1a] on the morphologic alterations of ocular disease might be of real pathophysiologic significance. This might apply not only to the eye but possibly to other tissues involved in disease and responsive to the action of pituitary adrenocorticotropic hormone. Finally, the importance of the eye in human endeavor and the limitations sometimes encountered in present day fever therapy in themselves are motivations for continued search for more rapid, effective and safe therapy.

The present investigation was undertaken, therefore, to demonstrate the possible action of pituitary adrenocorticotropic hormone on a variety of ocular lesions. The studies are continuing at the present time with attention now being directed to the chronic and degenerative diseases. We are concerned in this paper with the response to the drug of 7 patients with inflammatory lesions of the cornea and the uveal tract. A detailed report covering the present and extended investigations will follow.

From the Divisions of Ophthalmology, General Surgery and Metabolism of the Henry Ford Hospital.

The pituitary adrenocorticotropic hormone employed in these studies was made available through the cooperation of Dr. John R. Mote, medical director of the Armour Laboratories, Chicago.

Since this preliminary report was presented for publication an additional 25 patients have been treated. Both pituitary adrenocorticotropic hormone and cortisone have been used in lesions of the inflammatory group, with results comparable to those presented herein.

1. Markee, J. E.: Menstruation in Intraocular Endometrial Transplants in the Rhesus Monkey, Contrib. Embryol. **177**: 219, 1940.

1a. The term "action of pituitary adrenocorticotropic hormone" here and later implies that action which is mediated through its release of the adrenal cortical steroids.

CLINICAL MATERIAL

Cases for this study, with one exception, were drawn from the outpatient clinic of the Division of Ophthalmology of the Henry Ford Hospital. Patients were admitted to the inpatient service, where the detailed ophthalmologic study was made. All patients underwent extensive blood and urinary studies before, during and after the course of treatment, but results of these examinations will not be included in this preliminary report.

With one exception, a Negro woman aged 36 (case 2) all patients were over the age of 50, the oldest being a woman of 63 (case 3). In cases 1, 2, 4 and 6 the diagnosis of acute plastic iritis was made. In case 4, the acute plastic changes were superimposed on a chronic, bilateral, granulomatous iritis, and pulmonary roentgenologic observations led to a diagnosis of Böeck's sarcoid. In case 2 there were similar roentgenologic observations, but the latter diagnosis was not established. In case 3 severe keratitis had developed secondary to a recent cataract extraction. In case 5 a man aged 57 had acute chorioretinitis and an absolute cecocentral scotoma. In case 7 a man had severe keratitis, secondary iridocyclitis and secondary glaucoma. Minimal and inactive rheumatoid arthritis was present in case 1, and in case 6 the patient was treated during a period of severe bronchial asthma. In none of the patients did the history, physical examination and laboratory data suggest diabetes, renal disease or significant cardiovascular disease.

TREATMENT

The pituitary adrenocorticotropic hormone was administered intramuscularly at intervals of either four or six hours in dosages of 10 to 20 mg. Total dosages ranged from 185 to 432 mg., and treatment was continued over a period of three to thirteen days. The shortest duration of treatment was in cases 1 and 2 and the longest in case 3. In case 3 treatment was interrupted after seven days when the supply of the hormone became exhausted but was reinstituted eight days later with the arrival of a new supply. In cases 1 and 2 atropinization had been established prior to treatment with the hormone and was continued during the experimental therapy. In case 3 typhoid-induced fever was given while pituitary adrenocorticotropic hormone was unavailable. Analgesic and antimicrobial drugs were withheld from all patients except one (case 3), who received penicillin subconjunctivally during the period of induced fever. In all patients attempts were made to avoid early relapses by withdrawing the pituitary adrenocorticotropic hormone slowly over the last twenty-four to thirty-six hours of treatment.

RESULTS

The general effects of the pituitary adrenocorticotropic hormone will not be discussed except to say that the frequently observed exhilaration was noted in several of the patients and that the patient with bronchial asthma experienced prompt relief which continued throughout the period of observation.

The ophthalmologic results in this group of patients were striking. In all patients with regional pain and photophobia prompt relief was experienced. This

occurred as early as the second hour and in all patients was complete by the fourth hour after the initial dose of pituitary adrenocorticotropic hormone. In the patients with plastic iritis there was a significant reduction in cells and fibrin in the anterior chamber by the end of the fourth hour. Except in cases 6 and 7 the exudative features were resolved in twenty-six hours. In case 6, 150 mg. of the drug was required over a period of forty hours before the plastic exudate cleared completely from the anterior chamber. In case 7 230 mg. was required over a period of seventy hours before the plastic exudate resolved. In none of the cases of iritis did posterior synechiae develop. In cases 3 and 7, which involved keratitis, the corneal edema had disappeared at the end of twenty-four hours. In case 7, the patient with secondary glaucoma showed a progressive decline in ocular tension from 40 to 20 mm. of mercury (Schiötz) within the first twelve hours, and by the seventieth hour he had a tension of 12 mm. It is believed that this change coincided with the diminishing inflammatory process. The most striking response occurred in the case of chorioretinitis (case 5), in which the scotoma completely disappeared within four hours and the retinal lesion was completely resolved by the seventh day.

After treatment began, consistent changes were not observed in the conjunctival injection. This diminished progressively during treatment in some patients and resolved later in others. The hemorrhage in the anterior chamber in case 1 showed progressive absorption and disappeared by the forty-sixth hour.

Two patients (cases 1 and 2) were discharged from the hospital as "cured" and have been followed for seven and five weeks without evidence of relapse. In case 4 there was only an occasional cell in each anterior chamber five days after hormonal therapy was discontinued. Cases 5 and 6 in a short follow-up period have shown no regression. Treatment continues in case 7. The patient (case 3) in whom hormonal therapy was interrupted showed less response to the second course of treatment, which was stopped after a total of 432 mg. because of auricular fibrillation. This patient, when originally seen, was considered to have an incurable lesion, and subsequent examinations have revealed regression to the pretreatment level.

Transient glycosuria was observed in cases 3 and 5 while the patients were receiving pituitary adrenocorticotropic hormone. Fasting blood sugar levels and modified carbohydrate tolerance tests did not reveal significant hyperglycemia, and the glycosuria was considered to be of renal origin. In case 3 the fluid balance, body weight, physical examination, electrocardiograms and serum-electrolyte concentrations did not suggest a mechanism for the auricular fibrillation. Significant changes in the clotting times were observed in some patients, and further studies in this regard are now in progress.

REPORT OF CASES

CASE 1.—S. O., a white woman aged 48, was previously under our care in 1947 for acute plastic iritis of the right eye. The condition was arrested after eight days of typhoid vaccine therapy. On Dec. 13, 1949 she was readmitted to the hospital for acute plastic iritis of the same eye, after failing to respond for one week to ambulatory treatment. Examination revealed acute iritis with hemorrhage and a heavy plastic exudate in the anterior chamber. The only other significant physical observation was an inactive rheumatoid arthritis involving the joints of the fingers and the left shoulder. Treatment with pituitary adrenocorticotropic hormone was begun December 14 and continued for three days. Subjective findings of pain and photophobia disappeared at the end of four hours. At the same time slit lamp examination revealed a decided reduction and coagulation of the plastic exudate. Twenty-six hours after the initial injection of the drug the coagulum had disappeared and there remained only a few scattered cells and a residual of the blood clot in the anterior chamber. The clot completely disappeared at the end of forty-six hours. The remaining cells gradually decreased, and by the thirteenth day of observation the eye was entirely clear. It has remained clear to the time of this report.

CASE 2.—L. W., a Negro woman aged 34, was treated in 1948 in this hospital for acute plastic iritis of the left eye. After fever therapy the acute phase subsided, but she continued to show mild exacerbations which were treated in the outpatient clinic. She was readmitted with acute plastic iritis of the same eye on Dec. 24, 1949. Examination revealed severe circumcorneal injection with a 4 plus flare and a heavy plastic exudate in the anterior chamber. The only other significant physical observation was a roentgenogram of the chest interpreted as strongly suggestive of sarcoidosis. Subjective observations were severe photophobia and moderate pain. Administration of pituitary adrenocorticotropic hormone was started December 25 and continued for three days. Two hours after the initial dose, slit lamp examination revealed complete disappearance of the plastic exudate with a decided improvement of the subjective symptoms. Twenty-four hours later there was no flare and there were only a few cells in the anterior chamber. These few cells decreased during the remaining three days in the hospital. On the eleventh day there was only an occasional pigmented cell in the anterior chamber, and there has been no change since.

CASE 3.—M. S., a white woman aged 63, had severe keratitis nine weeks after a cataract extraction, right eye. Despite our impression that useful vision was lost in this eye, the patient was admitted to the hospital Dec. 28, 1949 for pituitary adrenocorticotropic hormone therapy. She had intense circumcorneal injection with bedewing of the cornea, more pronounced in the periphery. Descemet's membrane showed appreciable wrinkling. There was intense arborization of the deep vessels with extension about 2 mm. into the stroma just above the level of Descemet's membrane. The superficial vessels were invading to a lesser degree. The anterior chamber revealed a faint flare with a small number of cells. Subjectively, the patient complained of moderate pain, photophobia and lacrimation. Four hours after the initial injection of the drug all pain had disappeared and the central area was completely free of edema. In twenty hours there was no corneal bedewing and the corneal vessels were less engorged. Descemet's membrane showed early signs of clearing. The patient continued to improve during the next few days. Administration of the drug was discontinued on the eighth day because our supply was exhausted. Subjectively and objectively the ocular lesion showed almost immediate regression. Three injections of typhoid-H antigen and the repeated subconjunctival administration of penicillin over a period of eight days failed to bring improvement. A second course of pituitary adrenocorticotropic hormone was begun on the fifteenth day and continued for six days with only moderate improvement. The drug was discontinued when the patient manifested auricular fibrillation, which was readily controlled by quinidine sulfate. It was our impression that she had reached her maximum improvement from pituitary adrenocorticotropic hormone at the time the drug was discontinued. Examination one week after discharge showed that she had regressed to her pretreatment level.

CASE 4.—L. L., a Negro aged 55, was first treated for acute iritis of the left eye on Dec. 13, 1949. He responded well to fever therapy. When he was discharged December 19 the eye was entirely clear. Roentgen examination of the chest at that time was suggestive of sarcoidosis. Serologic reaction to the Kline test was 3 plus and to the Kahn test 1 plus. He returned Jan. 21, 1950 with typical bilateral chronic granulomatous iritis

and an acute plastic iritis superimposed in the left eye. Both corneas showed numerous small mutton-fat keratic precipitates. In the left eye there was a heavy fibrinous exudate with a 4 plus flare and many cells. The right eye showed only a few cells circulating in the aqueous. The patient complained of pain in the left eye and photophobia. Hormonal therapy was started January 22, and examination two hours later failed to reveal any fibrin in the anterior chamber of the left eye. Almost all pain and photophobia had subsided. Flare and cells were decidedly decreased. The right eye remained unchanged. After twenty-four hours the left eye was much clearer, and after four days of treatment most of the smaller keratic precipitates were thinning and crenating in both eyes. When discharged on the sixth day he showed continued improvement with only an occasional cell and the resolving keratic precipitates remaining. Admission and discharge roentgenograms of the chest showed no change in the observations that had been interpreted as sarcoidosis.

Case 5.—G. A., a white man aged 51, had been hospitalized in October 1949 for acute paracentral chorioretinitis of the right eye. The lesion resolved completely under fever therapy and histamine injections given alternately for seven days. On Jan. 21, 1950 he showed an acute exacerbation of this lesion. The fundus revealed a red, edematous lesion, slightly larger than 1 disk diameter and located just nasal to the macula. Tangent screens revealed an absolute cecocentral scotoma. Four hours after he received the initial injection of pituitary adrenocorticotropic hormone the scotoma had completely disappeared. Twenty-four hours later the lesion of the fundus began to clear. Seven days after treatment was started the fundus was completely clear except for a small area of depigmentation. Treatment in this case was continued for six days.

Case 6.—M. W., a white woman aged 50, was admitted on the allergy service of this hospital Jan. 20, 1950 for intractable bronchial asthma. The following day acute plastic iritis of the right eye developed. Examination on January 22 showed severe circumcorneal injection and an anterior chamber filled with cells and a heavy fibrin coagulum. The patient complained of severe pain and photophobia. This patient was purposely not atropinized. Two hours after the injection of 20 mg. of pituitary adrenocorticotropic hormone the patient was completely free of pain and showed no significant photophobia. By this time the plastic exudate had already begun to absorb and the bronchial asthma was decidedly improved. After four days, treatment with the drug was discontinued and the eye showed only an occasional cell in the anterior chamber. Despite lack of pupil dilatation synechiae had not formed. Five days after treatment was discontinued there was no recurrence of iritis or asthma.

Case 7.—G. R., a white man aged 62, was admitted to the hospital with severe keratitis and anterior uveitis of the right eye, of three months' duration. No history was available, but he apparently had received only local treatment. Examination revealed a nearly opaque cornea with bullous keratitis and early pannus formation. Even after instillation of glycerin it was impossible to determine the exact amount of exudate in the anterior chamber, but large mutton-fat keratic precipitates were present in the central corneal area. Tension of the right eye was 40 mm. of mercury (Schiötz). The pupil would not dilate, posterior synechiae apparently being present. There was mild pain.

Pituitary adrenocorticotropic hormone therapy was begun Jan. 26, 1950. Four hours later the pain had subsided. At the fifth hour the edema was noticeably less, and both the bullae and edema had disappeared at the end of the sixth hour. Tension was reduced to 20 mm. of mercury after eleven hours. Better visualization of the anterior chamber at this time revealed a heavy plastic exudate, which steadily subsided over the next twenty hours. Tension varied between 10 and 20 mm. of mercury. After five days of hormonal therapy the corneal stroma had cleared moderately. As the patient is still receiving treatment it is impossible to say whether these improvements will regress when hormonal therapy is discontinued.

COMMENT

It would appear from these preliminary studies that pituitary adrenocorticotropic hormone significantly and favorably alters some inflammatory diseases of the uveal tract. It is apparent that the rapidity and completeness of its action in the more acute inflammatory cases exceeds the most favorable response achieved with present day methods of therapy. Longer periods of observation are necessary to evaluate the role of this agent in chronic inflammatory diseases. In contrast to fever therapy the patients experience no discomfort. The limitations which are sometimes encountered in the treatment of inflammatory ocular lesions, both in the elderly patient and in the person with complicating disease precluding fever therapy, appear to be overcome in part by the results of these studies. However, it is too early to arrive at more than tentative conclusions, and further study is obviously necessary before any final opinions can be written. The manifold action of pituitary adrenocorticotropic hormone is such that limitations to its use in such diseases may be encountered. The occurrence of renal glycosuria in 2 patients, though transient and slight, and auricular fibrillation in 1 patient, though not established as a true complication, supports this belief. Some optimism in this regard is justified, however, in view of the rapid remissions of the lesions in some of our patients, thus requiring a minimal dosage. Although this is only a preliminary impression, we believe that a gradual reduction in the dosage of pituitary adrenocorticotropic hormone was helpful in preventing the occurrence of relapses during the period of adrenal hypofunction which may follow withdrawal of the hormonal preparation.

Finally, we would like to emphasize one of the considerations which motivated the present investigation. The eye with its inflammatory, exudative and proliferative diseases offers, in particular, an excellent opportunity to observe the action of pituitary adrenocorticotropic hormone in these pathologic processes. It has effected here a rapid resolution of hemorrhage, fibrinous and cellular exudates, thus visually demonstrating the importance of this hormonal agent in the response of the organism to these features of disease.

SUMMARY

A preliminary report on the action of pituitary adrenocorticotropic hormone in certain inflammatory diseases of the eyes has been presented. To date, 7 patients with acute and chronic lesions have been followed. Four patients had acute plastic iritis and 2 had keratitis and anterior uveal tract involvement, 1 of the 2 with secondary glaucoma. One patient had a recent chlorioretinitis with absolute scotoma. All patients responded abruptly and favorably to hormonal therapy. Symptomatic relief and distinct objective changes were achieved as early as the second hour in 1 patient and by the fourth hour in the other patients. The patient with chorioretinitis and associated scotoma was free of the latter by the fourth hour. The patient with keratitis secondary to cataract extraction responded favorably to the drug but improvement regressed when treatment was withdrawn. The second patient with keratitis has responded favorably and is still receiving treatment. Dosages employed ranged from 185 to 432 mg. over a period of three to thirteen days. Glycosuria in 2 patients and auricular fibrillation in 1 patient were observed during the period of administration of pituitary adrenocorticotropic hormone.

USE OF PITUITARY ADRENOCORTICOTROPIC HORMONE (ACTH) IN POLIOMYELITIS

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Certain data about poliomyelitis suggest an unusual host-parasite relationship. Among these are the low incidence of paralysis,[1] less than 1 in 100 cases of poliomyelitis infection; the familial incidence,[2] constitutional factors [3] and endocrine imbalance theories [4] which have been advanced to explain susceptibility; excessive fatigue and chilling or exhaustion during the incubation period, which is frequently followed by severe paralysis, and the greater incidence of paralysis in pregnant women as compared with nonpregnant women.[5] The concept of latent immunization to various antigenic types of virus does not explain the epidemiologic patterns of the disease.[6] All these observations suggest that susceptibility or resistance to poliomyelitis involves nonspecific defensive mechanisms and, indirectly, that the host response is more important than the virulence of the virus in determining the course of infection. Rapid mobilization of bodily defensive mechanisms may limit the spread of infection in the usual nonparalytic case, whereas a slower response as a result of constitutional factors or exhaustion may permit infection to spread. Indeed we do not know whether or not poliomyelitis precipitates an "alarm reaction." Pituitary adrenocorticotropic hormone (ACTH) induces this reaction quickly, and it occurred to us that a failure of these mechanisms to act naturally might contribute to the development of paralytic poliomyelitis.

For these reasons, the therapeutic use of pituitary adrenocorticotropic hormone in early poliomyelitis seemed worthy of trial. Ideally, one should test this theory by giving the drug during the first few days of the incubation period, and it is fully realized that its use after the disease is manifest may prove nothing. However, with the encouragement of Dr. John R. Mote of the Armour Laboratories, a cautious therapeutic trial was made, and this led to the study reported herein. It was believed that the following questions might be answered: (1) Is the "alarm reaction" evoked by poliomyelitis? (2) What is the physiologic action of pituitary adrenocorticotropic hormone in poliomyelitis? (3) Does the drug modify the course of poliomyelitis when administered early in the course of the disease?

Single doses of varying amounts of the agent were given to a number of poliomyelitis patients at the Camden Municipal Hospital. Deleterious effects were not observed, so 2 patients were given a daily maintenance dose of 50 mg. for four days. In both patients the temperature returned to normal within twelve hours and the progression of paralysis ceased. The apparent absence of toxic effects in these patients suggested that a definitive trial with a significant number of patients should be run without waiting for further animal experiments. Since only sporadic cases were occurring in southern New Jersey, the study was moved to the Children's Medical Center at Boston, where an extensive epidemic was in progress.

TABLE 1.—*Dosage Schedule of Pituitary Adrenocorticotropic Hormone in Milligrams per Day Divided into Four Equal Doses and Administered Intramuscularly*

	Day of Therapy			
Weight in Kilograms	1	2 (R_2)	3	4
Under 20	40	40	20	20
20 to 40	60	60	40	20
40 to 60	80	80	60	40
Over 60	120	100	80	60

The first 18 patients (R on the accompanying chart) received the drug as shown above.
The next 17 patients (R_2 on the chart) were maintained at the dosage shown for the second day of therapy in this table for a period of five days.

PLAN OF STUDY

To be admitted to the study, patients were required to present at least four of the seven criteria set forth by the National Foundation for Infantile Paralysis, namely, history, fever, stiff neck, stiff back, not less than 10 or more than 500 cells in the cerebrospinal fluid, elevated level of protein in the cerebrospinal fluid and demonstrable muscle weakness. In addition, we required that patients must have been ill less than five days and have a temperature of 100.5 F. or more. A total of 70 patients were studied, 35 receiving pituitary adrenocorticotropic hormone and 35 a placebo.

Patients admitted to the study were given the drug or a placebo as determined by random selection through drawing balls of two colors from a container. All medication was given intramuscularly at six hour intervals for four or five days. The identity of the medicament was unknown to the nursing and medical staffs who cared for and evaluated the patients. The dosage schedule of the adrenocorticotropic agent is shown in table 1.

For the first part of the study crystalline penicillin was used as the placebo. This was later changed to isotonic sodium chloride solution when it was pointed out by Dr. Peter Forsham that the eosinophil count might be altered in persons hypersensitive to penicillin.

The criteria for activity of the drug and adequacy of dosage were obtained by eosinophil counts done initially and at four hours, then daily during therapy and for

Aided by a grant from the National Foundation for Infantile Paralysis.
The pituitary adrenocorticotropic hormone (ACTH) used in this study was supplied by Dr. John R. Mote of the Armour Laboratories.
Dr. Charles Janeway assisted in these studies by making available the facilities of the Children's Medical Center, by coordinating administrative details and by giving technical advice.

From the Municipal Hospital, Camden, N. J. (Drs. Coriell and Murphy) and from the Children's Hospital of Philadelphia (Department of Pediatrics, University of Pennsylvania School of Medicine), Philadelphia (Drs. Coriell, Murphy and Stokes); from the Division of Clinical Laboratories, Children's Hospital, and the Department of Pediatrics, Harvard Medical School, Boston (Dr. Siegel), and from the Department of Pediatrics, Children's Medical Center, Harvard Medical School (Dr. Cook).

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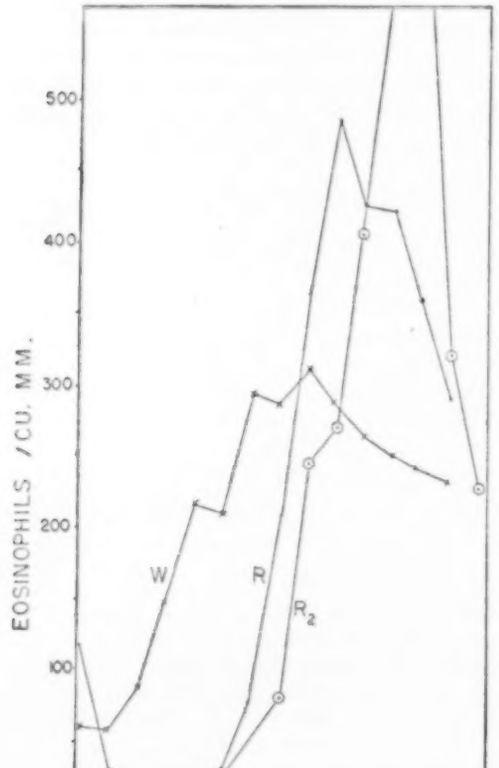
eight days after discontinuing therapy, by excretion of 17-ketosteroids and by blood chemical studies of the sodium, potassium and fasting blood sugar levels when indicated.

Clinical evaluation of patients was by the medical staff and was tabulated daily by one of us (A. S.) on prepared forms. Only objective criteria were used. These included the temperature response, progression or remission of paralysis, muscle spasm and tenderness and later orthopedic follow-up for recovery from residual paralysis. Paired serum and stool specimens were collected from a number of patients and stored for future use.

RESULTS

The total number of cases in the study appears to be adequate to give a definite and clearcut answer to the questions posed. As shown in table 2, the median



Eosinophil response in poliomyelitis: *W*, average count of 35 patients who received a placebo every six hours for four days; *R*, average count of 18 patients who received pituitary adrenocorticotropic hormone in decreasing doses every six hours for four days, and R_2, average count of 17 patients who received a constant dose of the hormone every six hours for five days. The base line indicates the time after therapy.

day of hospitalization was almost identical for the two groups, as was the distribution of paralytic and nonparalytic cases. Practically every patient had a low eosinophil count an admission. Two patients who later died had zero eosinophil counts on admission. In the control group the eosinophil count rose gradually to normal levels on the second hospital day, with a continued rise or rebound to higher levels on the fifth to seventh day. The group receiving pituitary adrenocorticotropic hormone had a sharp drop in the eosinophil count four hours after the first dose, and the count remained down until the drug was discontinued, when a more decided rebound occurred. The average eosinophil count of each group is plotted in the accompanying chart, which also shows that the rebound of eosinophils was delayed one day longer in the 17 patients who received the drug for five days instead of four days. The higher initial eosinophil count in the group which received the drug is caused by 1 patient who had an initial count of 2,100 per cubic millimeter.

TABLE 2.—*Distribution of Cases*

	Control	Pituitary Adrenocorticotropic Hormone
Total number	35	35
Median day of hospitalization	2.6	2.5
Nonparalytic	13	12
Paralytic	22	23
Percentage paralyzed	63	66
Deaths	0	1

If this count is omitted both groups have an average initial count between 50 and 60 per cubic millimeter.

Excretion of 17-ketosteroids was determined in 11 patients. The first twenty-four hour urine specimen was collected on the second day of hormonal therapy and the control specimen on the tenth hospital day, five or six days after therapy was discontinued. The results shown in table 3 are somewhat variable, but it seems clear that the control cases had no increased 17-ketosteroid excretion in the two specimens tested. With 1 exception, patients treated with the hormone had higher levels in the first specimen while under the influence of administration of the adrenocorticotropic substance.

We concluded from the eosinophil counts and 17-ketosteroid excretion levels that the dosage of pituitary adrenocorticotropic hormone was adequate to produce a physiologic effect.

The course of the disease in individual patients was extremely variable, and in some patients use of the hormonal agent seemed to have effected a dramatic termination of fever and paralysis. In fact, after we

TABLE 3.—*Urinary Excretion of 17-Ketosteroids, Milligrams per Twenty-Four Hours*

Name	Age	Sex	Medication *	Hospital Day 2	Hospital Day 10
E. L.	15	M	Treated	16.1	4.87
P. F.	7	F	Treated	2.20	0.34
B. M.	13	M	Treated	14.3	6.55
W. W.	7	M	Treated	1.72	1.61
H. D.	16	M	Treated	32.6	13.81
R. R.	9	M	Treated	5.92	3.65
K. W.	24	M	Treated	12.41	12.6
G. E.	6	M	Control	1.08	1.06
E. H.	6	M	Control	1.10	0.55
R. S.	7	M	Control	2.05	1.9
W. S.	8	M	Control	1.17	0.9

* Treated patients received pituitary adrenocorticotropic hormone; controls received crystalline penicillin solution or isotonic sodium chloride solution.

had treated 7 patients in each group it appeared that the 7 receiving the pituitary adrenocorticotropic hormone were benefited. Here we wish to stress the fallacy of drawing conclusions from a few cases, for with increased numbers of patients it became quite clear that there was no detectable difference between the two groups. Table 4 shows the distribution of cases on the basis of clinical type of poliomyelitis.

In table 5 it is obvious that the average days of fever in the control and treated groups was 5.6 and 5.7 days, respectively, and the average days of fever after treatment was 2.9 and 2.8 days. Paralysis progressed in the control group for 4.5 days from onset and for 2.4 days after treatment was started, and in the treated group the figures were 4.4 days from onset and 2.2 days after treatment.

Frequent examination of patients by members of the orthopedic staff of the Children's Medical Center did not reveal any difference between treated and control patients in the degree of spasm, pain and tenderness or the duration of the sensitive stage. The long-term follow-up of these patients is being carried out.

SUMMARY

The "alarm reaction" is mobilized in poliomyelitis as shown by the eosinophil response. In these patients, pituitary adrenocorticotropic hormone (ACTH) produced a physiologic effect as evidenced by a further depression of the eosinophil count and by increased excretion of 17-ketosteroids. There was no demonstrable effect in the treated as compared to the untreated group when evaluated on the basis of (1) temperature response, (2) paralysis, (3) progression of paralysis or (4) early residual effects.

Statistical analysis shows clearly that pituitary adrenocorticotropic hormone has no beneficial or obvious deleterious effect on the course of poliomyelitis when treatment is begun after the onset of symptoms.

TABLE 4.—*Number of Cases of Poliomyelitis of Various Clinical Types*

	Control	Pituitary Adrenocorticotropic Hormone
Nonparalytic	13	12
Spinal without respiratory involvement	13	16
Spinal with respiratory involvement	0	1
Bulbar without respiratory involvement	8	4
Bulbar with respiratory involvement	1	2
Total	35	35

TABLE 5.—*Average Days of Fever and Paralysis Progression in Treated and Control Groups*

	Fever *				Paralysis *			
	Total		After Treatment		Total		After Treatment	
	W	R	W	R	W	R	W	R
Nonparalytic	5.0	5.3	2.9	3.0	...	...	...	...
Spinal	5.7	5.7	2.8	3.1	5.4	4.8	2.7	2.9
Bulbar	6.2	6.0	3.0	2.3	3.7	3.9	2.2	1.6
Average	5.6	5.7	2.9	2.8	4.5	4.4	2.4	2.2

* W indicates the control patients who received the placebo, R the treated patients who received pituitary adrenocorticotropic hormone.

Physicians as Citizens.—Physicians, as good citizens, possessed of special training, should advise concerning the health of the community wherein they dwell. They should bear their part in enforcing the laws of the community and in sustaining the institutions that advance the interests of humanity. They should cooperate especially with the proper authorities in the administration of sanitary laws and regulations.—Section 1, Chapter IV of the PRINCIPLES OF MEDICAL ETHICS of the American Medical Association.

LIFE SITUATIONS, EMOTIONS AND HYPERINSULINISM

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In December 1942 I presented for the opening meeting of the American Psychosomatic Society a preliminary report on "A Mechanism of Fatigue in Neuropsychiatric Patients." [1] Subsequently, Alexander and I [2] reported a psychosomatic study of hypoglycemic fatigue. This latter communication and the preliminary report were confined to describing a well defined group of psychoneurotic patients with an associated peculiarity of carbohydrate metabolism, manifested by flattening of the intravenous dextrose tolerance curve, as in hypoglycemia. The psychologic condition can be described best as an asthenic syndrome, the outstanding features being apathy, loss of zest, a general let-down feeling of aimlessness and revulsion against the routine of everyday life, be it occupational or household duties. Seldom is this apathy connected with anxiety or a pronounced depression. Another constant feature is fatigue, chronic or appearing in acute attacks. The fatigue has certain fairly constant features. It is present as a rule on awakening, becomes slightly more severe by midmorning, temporarily improves after luncheon and is most marked in midafternoon. There is practically always complete relief after the heavy evening meal. The patient may awaken with a severe headache, which is manifest also during the midafternoon fatigue. Along with this chronic fatigue there may be acute attacks of extreme weakness, tremulousness, sweating and vertigo. At times a feeling of "lightheadedness" may be manifest. The acute attacks may be associated with anxiety of fainting or free-floating anxiety.

Spontaneous hypoglycemia has been noted by many investigators, who have attempted to define the variety of settings in which it occurs. Harris,[3] Ross and Josephs,[4] Wauchope,[5] Conn, Wilder and others have reviewed the subject.

The blood sugar level may fall after interference with any one of several factors in the normal homeostatic mechanism. Hepatic disease and disease of the pancreas, either from known adenoma or from hyperplasia of the islands of Langerhans, have been cited as important factors which may cause spontaneous hypoglycemia. Faulty diet, including errors in intake of carbohydrates and the lack of assimilable vitamins, also has been a known factor. The pituitary-adrenal syndromes of Simmonds' disease and Addison's disease have long been recognized as associated with hypoglycemic manifestations. Rennie and Howard [6] studied hypoglycemia and tension depression in neuropsychiatric cases. With their oral dextrose tolerance test they discovered the so-called flat curves and found that when the patients were recovering from their tension depressive symp-

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1. Portis, S. A., and Zitman, I. H.: A Mechanism of Fatigue in Neuropsychiatric Patients, J. A. M. A. **121**: 569 (Feb. 20) 1943.

2. Alexander, F., and Portis, S. A.: A Psychosomatic Study of Hypoglycaemic Fatigue, Psychosom. Med. **6**: 191 (July) 1944.

3. Harris, S.: Hyperinsulinism and Dysinsulinism, J. A. M. A. **83**: 729 (Sept. 6) 1924; Hyperinsulinism and Dysinulinism (Insulogenic Hypoglycemia), Internat. Clin. **1**: 9 (March) 1932.

4. Ross, S. G., and Josephs, H. W.: Metabolism of Recurrent Vomiting, Am. J. Dis. Child. **28**: 447 (Oct.) 1924.

5. Wauchope, G. M.: Hypoglycemia: Critical Review, Quart. J. Med. **2**: 117 (Jan.) 1933.

6. Rennie, T. A. C., and Howard, J. E.: Hypoglycemia and Tension-Depression, Psychosom. Med. **4**: 273 (July) 1942.

toms the oral dextrose tolerance curve returned to near normal.

I was interested in this hypoglycemic stage of the disease because so-called pernicious inertia was the most prominent symptom of a patient who was referred to me by a neuropsychiatrist and of a group of patients later seen in the office. I therefore undertook a study of the underlying metabolic processes, particularly as they affected dextrose metabolism, to see whether I could not in some way determine the factors which produced the hypoglycemia.

SURVEY OF THE LITERATURE

Although many factors are involved in the homeostatic mechanisms which maintain blood sugar levels, those mechanisms associated with the insulin regulatory system are most important to this study.

The exact manner in which the secretion of insulin is controlled is as yet undetermined. Two main theories have been propounded to explain this phenomenon: the neurogenic and the humoral. Unfortunately, neither explains all the various manifestations. Proof must come from indirect determinations, since the quantity of insulin present in the blood stream is too low to be determined by chemical means or biologic assay.

Neurogenic Theory.—That both myelinated and nonmyelinated nerve fibers supply the islands of Langerhans was demonstrated in 1902 by Gentes.[7] Further, it was shown by McCrea [8] that these fibers are in communication with branches of the right vagus nerve.

Many workers have observed the effects of stimulation of the right vagus nerve on the blood sugar level. Britton [9] reported a decrease in blood sugar following such stimulation. However, this occurred only when the pancreatic vein was intact. An increase in insulin secretion into the pancreatic duodenal vein after vagal stimulation was noted by Dietrich.[10]

A fundamental contribution was made by Clark,[11] who reported that drugs which stimulate the parasympathetic nervous system produce a fall in the blood sugar level of intact rabbits; this effect did not occur after section of the vagus nerve.

The foremost proponents of the vagal stimulation theory have been La Barre and his associates,[12] who reported that the normal dextrose level of a dog may be reduced by transfusion of blood from the pancreatic vein of another animal during stimulation of its right vagus nerve.

Pursuing this problem further, these same investigators [13] seem to have established that a center in the thalamus stimulates the pancreatic secretion of insulin when the blood sugar rises, impulses being transmitted through the vagus tracts to the islet tissue. Using 3 dogs with isolated circulatory and nervous systems, they discovered that, although removal of the cerebral hemispheres did not prevent the hyperinsulinism resulting from transfusion of hyperglycemic blood through the isolated head, removal of the thalamus did abolish this hyperinsulinism. However, Gayet and Guillaumie [14] were unable to confirm these results.

Humoral Theory.—Those who support the theory of humoral control believe that the blood sugar level acts directly on the pancreas to control insulin secretion. This view has been given support by the work of Phillips,[15] who reported that vagotomy has no effect on sugar tolerance, and by Long and Fry,[16] who claimed that glycogen resynthesis in muscle is not influenced by section of the vagi.

Houssay and his co-workers [17] have shown that the pancreas can produce its own internal secretion after all its extrinsic nerve supply has been removed and that the control of insulin secretion is directly dependent on the blood sugar level. Most workers seem to agree that the blood sugar level is the primary factor but that the neurogenic factor serves in emergencies.

Not much evidence substantiates the claim that the secretion of insulin is dependent on other hormones produced by the endocrine glands, with their secretion in turn controlled by the blood sugar level.

The presence of a "pancreatropic" factor in the pituitary gland has been claimed by some, while others have expressed the belief that thyroid extract sensitizes the islet cells for the secretion of insulin.

A more comprehensive view has been taken by Soskin and his collaborators,[18] who have stated the opinion that the output of insulin is relatively constant, with a homeostatic blood sugar–regulating mechanism depending primarily on the liver and controlled by the opposing influences of the pituitary, adrenal and pancreatic hormones.

EXPERIMENTAL EVIDENCE

In view of these theories and the fact that the psychoneurotic patients studied showed hypoglycemia as an important factor in their fatigue, I searched for further light on this hypoglycemic factor in man. There is voluminous psychiatric and medical literature concerning the effect of emotional impulses on the somatic system. It is well known also that continued physiologic activity in a tissue may lead to either hypertrophy or hyperplasia, depending on the type of tissue.

Since the pancreas is an end organ and subject to vagal stimulation, I considered it logical to assume that the hypoglycemia of psychoneurotic patients is due to long-continued stimulation of the right vagus nerve. This assumption was based on the hypothesis that emotional processes occur somewhere in the highly integrated cortical centers and that the emotional impulses first go through the hypothalamus and are relayed to the sympathetic and parasympathetic portions of the autonomic nervous system. During fatigue, the stimulation by emotional impulses traversing this pathway would be nearly constant. It might even be possible that certain emotions would follow definite pathways in the nervous system, localizing in particular organs, and this stimulation might lead to increased

7. Gentes, M.: Notes sur les terminaisons nerveuses d'ilots de Langerhans du pancreas, Compt. rend. Soc. de biol. **54**: 212, 1902.
8. McCrea, E. D. A.: The Abdominal Distribution of the Vagus, J. Anat. **59**: 18, 1924-1925.
9. Britton, S. W.: Studies on the Conditions of Activity in Endocrine Glands, Am. J. Physiol. **74**: 291 (Oct.) 1925.
10. Dietrich, S.: Untersuchungen über Diabetes und Insulinwirkung: XII. Der direkte Nachweis der Insulinsekretion des Pancreas, Arch. f. exper. Path. u. Pharmakol. **125**: 336, 1927.
11. Clark, G. A.: The Influence of the Vagus on the Islets of Langerhans: I. Vagus Hypoglycemia, J. Physiol. **59**: 446 (March) 1925.
12. La Barre, J.: Sur l'augmentation de la teneur en insuline du sang veineux pancréatique après excitation du nerf vague, Compt. rend. Soc. de biol. **96**: 193 (Jan. 28) 1927.
13. La Barre, J.: The Role of the Central Nervous System in the Control of Pancreatic Secretion: I. The Secretion of Insulin During Hypoglycemia, Am. J. Physiol. **94**: 1-13 (July) 1930.
14. Gayet, R., and Guillaumie, M.: Expériences concernant l'effet de l'excitation électrique du vague sur l'insulino-sécrétion, Compt. rend. Soc. de biol. **112**: 1197 (April 1) 1933.
15. Phillips, R. A.: The Influence of the Vagus Nerve on the Glycemic Level, Am. J. Physiol. **105**: 257 (Aug.) 1933.
16. Long, C. N. H., and Fry, E. G.: The Effects of Vagotomy on Muscle Glycogen Resynthesis, Am. J. M. Sc. **185**: 884 (June) 1933.
17. Houssay, B. A.; Lewis, J. T., and Foglia, V. G.: La fonction endocrine du pancréas normal ou énervé pendant l'hypoglycémie insulinique, Compt. rend. Soc. de biol. **101**: 239 (May 24) 1929.
18. Soskin, S.; Allweiss, M. D., and Cohn, D. J.: Influence of the Pancreas and Liver on the Dextrose Tolerance Curve, Am. J. Physiol. **109**: 155 (July) 1934. Soskin, S.; Mirsky, I. A.; Zimmerman, L. M., and Heller, R. C.: Normal Dextrose Tolerance Curves, in the Absence of Insulin, in Hypophysectomized Depancreatized Dogs, Am. J. Physiol. **114**: 648 (Feb.) 1936.

activity and irritability of the cells of the islands of Langerhans. The manifestation might be temporary or prolonged, depending on the degree and duration of the psychic and emotional impulses.

In order to establish the validity of this assumption, I studied a large group of patients whose outstanding symptom was fatigue, which could not be explained by thorough physical and routine laboratory investigation, including a determination of blood sugar during fasting. However, because of the fairly constant periodicity of the fatigue, a relation to carbohydrate level was sought. This was suggested by the flat intravenous dextrose tolerance curve of the first patients studied, in the absence of any of the known causes, including islet cell adenoma of the pancreas.

To obtain evidence of changes in the carbohydrate metabolism, the standard intravenous dextrose tolerance test described by Soskin was used. Since gastrointestinal motility is readily influenced by emotional factors and the rate of absorption of dextrose from the gastrointestinal tract is affected by motility and by cellular changes in the wall of the intestine, the oral dextrose tolerance test was not considered suitable in

TABLE 1.—*Mean, Standard Deviation and Coefficient of Variation of Blood Sugar Tolerances in 157 Patients with Fatigue and in 772 Controls* *

		Mean	Standard Deviation	Coefficient of Variation
(Flat)	Fasting	78	12	15
	½ hr.	100	4	4
	1 hr.	81	15	17
	1½ hr.	73	14	18
	2 hr.	70	13	18
	3 hr.	75	13	17
(Control)	Fasting	85	12	14
	½ hr.	147	26	17
	1 hr.	112	21	18
	1½ hr.	91	17	18
	2 hr.	81	14	17
	3 hr.	83	21	25

* These figures reveal that the most significant differences occur at the 30 and 60 minute levels of blood sugar, the 30 minute being the most significant. (See text)

a metabolic investigation affecting mechanisms of blood sugar control. Furthermore, the initial increase of blood sugar is far greater with the intravenous than with the oral test, so that one can logically expect a greater immediate response in secretion of insulin. The technic used for the intravenous dextrose tolerance test is as follows:

The patient presents himself after a twelve hour fast (no morning bath, no water by mouth except for oral hygiene) and is weighed. A blood sample for determining fasting sugar is withdrawn. The patient is then given 0.33 Gm. of 50 per cent dextrose per kilogram of body weight with a large syringe (50 or 100 cc. type). The time for administration is usually between two and five minutes, depending on the age of the patient. Samples of blood are then withdrawn at 30, 60, 90, 120 and 180 minute intervals (Somogyi method of true blood sugar determination). The results of these values are noted and charted. (The amount of sugar in the urine was not determined during the test, because no clinical significance appeared to be attached to the results.)

Care must be exercised to prevent stagnation of venous blood during the taking of any one sample.

This test was performed on 929 patients, of which 157 had a so-called flat curve (table 1, fig. 1).

This series comprised a group of patients who had consulted me for complaints in which psychogenic factors played a more or less predominating role. I was interested in studying the carbohydrate metabolism not only of patients suffering only from fatigue but of a larger group of patients with psychosomatic problems. While there was only slight variation in the fasting blood sugar between the two groups, there was a marked difference in blood sugar level thirty minutes after injection. In not one of the 929 patients did the third

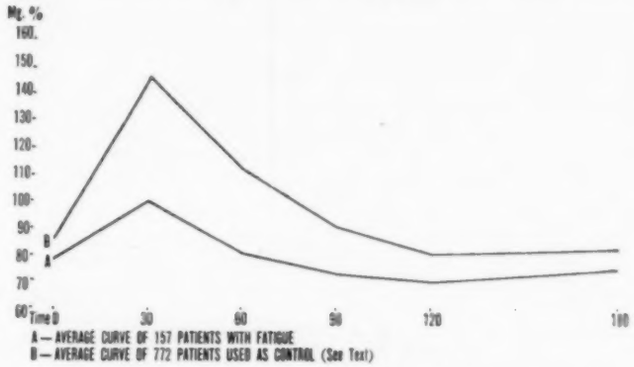

Fig. 1.—Intravenous dextrose tolerance test of fatigue and control groups.

hour level reach the original fasting level. This is important in studying the carbohydrate metabolism of emotionally disturbed persons.[19] In the fatigue group, because of the low level at thirty minutes, the curves were flat in comparison with those in the other group. The term "flat curve" is justifiable in comparison with the curves of both normal persons and patients without fatigue as a predominating symptom. Therefore, the finding is significant in the clinical picture of the syndrome previously described. Alexander and I have already reported that these values represent relative hypoglycemia:

The term hypoglycemia refers ordinarily to blood sugar values consistently below the average normal range. Thus, it covers values below 60 mg.%. The signs and symptoms of the hypoglycemic syndrome appear generally when the blood sugar level reaches < 30-40 mg.%. However, it has been observed experimentally and clinically that the typical symptoms may appear at levels of 100 mg.% (Mann in depancreatized dogs, also adrenalectomized animals), or may not be present even

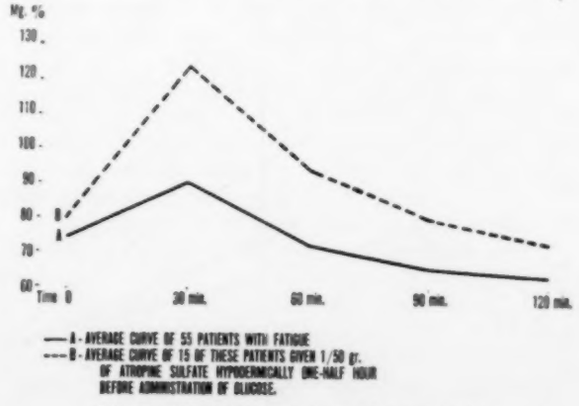

Fig. 2.—Intravenous dextrose tolerance tests.

when the blood sugar has almost vanished from the blood (case of Parnas and Wagner with blood sugar of 0 for days). The precise relation between blood sugar level and central nervous system symptoms in any particular case is not understood at present.

Cases which present symptoms analogous to the hypoglycemic syndrome and which are benefited by a rise in blood sugar—

19. Portis, S. A.: Idiopathic Ulcerative Colitis: Newer Concepts Concerning Its Cause and Management, J. A. M. A. **139**: 208 (Jan. 22) 1949.

even though these symptoms are present at blood sugar levels normal for other persons—may for the sake of uniformity and a working hypothesis be termed "relative" hypoglycemia. The term relative would express the supposition that these particular persons have "normal" blood sugar levels which are "hypoglycemic" for them (for their central nervous system).

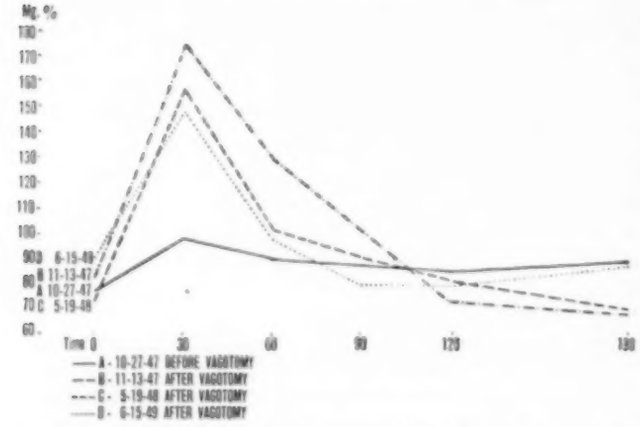

Fig. 3.—Intravenous dextrose tolerance tests before and after vagotomy.

The hypoglycemia due to islet cell adenoma of the pancreas is, as a rule, more severe than that seen in functional hyperinsulinism. For instance, the fasting and two hour blood sugar levels are usually below 40 mg., a level never seen among fatigue patients with functional hyperinsulinism. Furthermore, the initial fasting level of fatigue patients is only between 6 and 10 mg. below that of normal persons.

If the "flat curves" are the result of increased stimulation of the right vagus nerve, then paralysis of the vagus nerve with atropine sulfate should abolish this influence. Fifteen of the first 55 patients (fig. 2) were treated in the following manner:

A sample of the fasting blood was taken, as previously described. The patient was then given 1/50 grain (1.3 mg.) of atropine sulfate hypodermically. After a half hour for adequate

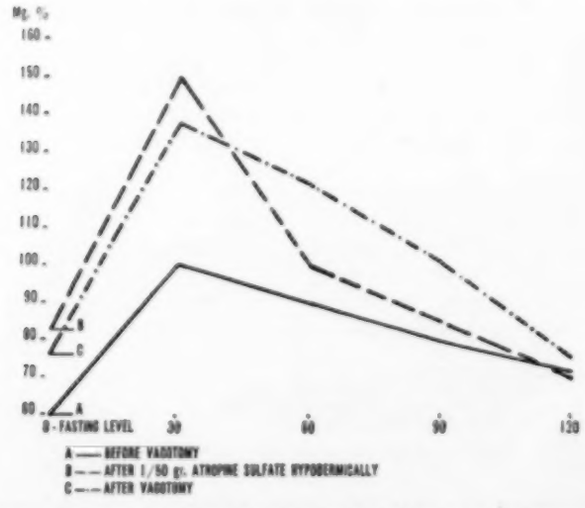

Fig. 4.—Intravenous dextrose tolerance studies before and after vagotomy.

pharmacologic action of the drug, another blood sample was withdrawn. Immediately thereafter 50 per cent dextrose was injected as in the previous test, which had given a "flat curve," and blood samples were withdrawn at the usual intervals.[20]

20. Portis, S. A.: The Medical Treatment of Psychosomatic Disturbances, J. A. M. A. **126**: 413 (Oct. 14) 1944.

In these 15 atropinized patients, the thirty minute blood sugar level resembled that of normal persons. Because of the uniformity of results in this group, I felt that there was no need to subject a large group to this test.

Although flattening of the intravenous dextrose tolerance curve is rare among patients with peptic ulcer, 2 patients with a flat curve were studied before and after subtotal gastrectomy and high infradiaphragmatic vagectomy. Tables 2 and 3 and figures 3 and 4 show that the half hour blood sugar levels after complete vagectomy were even higher than those of atropinized patients. Furthermore, in 1 case this return to a near normal curve had persisted for more than a year at the time this report was written (fig. 3).

On the basis of these laboratory data, I believe that the fatigue in the patients studied is due to relative hypoglycemia, which is presumably related to some emotional situation characterized by loss of spontaneous zest and revulsion against routine activities. This results in a disturbance of the homeostatic mechanism regulating the blood sugar concentration. Such a mechanism is probably responsible for the chronic asthenic syndrome and for occasional attacks of weakness and fatigue. Apparently the emotional tension to which

TABLE 2.—*Intravenous Dextrose Tolerance Test Before and After Vagotomy*

	Before Vagotomy 10/27/47	After Vagotomy 11/13/47	After Vagotomy 5/19/48	After Vagotomy 6/15/49
Fasting	77	82	73	90
30 min.	98	175	157	149
60 min.	90	130	102	98
90 min.	..	..	91	80
120 min.	85	73	82	80
180 min.	90	69	71	88

one ordinarily refers as zest, enthusiasm or interest keeps up the tonus of the vegetative innervations, maintaining a balance between the sympathetic adrenal and the parasympathetic insular tonus. If one could extend Cannon's fundamental observations, one might assume that outwardly directed activity of the organism in which it participates with enthusiasm, zest and spontaneous striving has a tuning up effect on the sympathetic adrenal system which is qualitatively similar to that of fear and rage. Fear and rage are extreme conditions in which the organism is tuned up for an outwardly directed activity in an emergency.

The main function of the autonomic nervous system is to adapt the internal vegetative functions of the organism to the tasks it is called on to perform. On the basis of these observations it may be assumed that, like rage and fear, a keen enthusiastic striving for a goal may have a similar, more prolonged but less intensive tuning up effect on the internal vegetative processes. It is probable that without such a tuning up, sustained effort could not be carried out with economy. It is well known that perfunctory activity performed without emotional participation is more fatiguing than even strenuous activity performed with emotional participation. Clinical observations seem to indicate that fatigue and apathy developing during activity performed without interest are not merely subjective emotional states but are based on the lack of adaptation of the carbohydrate metabolism to the effort required from the organism. Apparently the brain needs adequate dextrose at all times for its physiologic balance. When relative hypoglyoemia super-

venes, the brain will not exteriorize its emotional patterns to a degree compatible with a stable emotional household. Apparently the neuron reacts to the first drop in blood sugar by becoming irritable, and only when the blood sugar has been low for a long time does the neuron become unresponsive (hypoglycemic coma).

TREATMENT

These observations led to the development of a therapeutic approach to the problem.

Diet.—To insure against the giving of too much readily absorbable carbohydrates in the form of simple sugar, the following diet was outlined:

Diet Suggested for Fatigue Patient

Foods Allowed:

Cereals:	All types, preferably whole grain, cooked or dry, one serving daily
Bread:	Enriched white, whole wheat or rye bread (white crackers, melba toast or Holland rusk if desired)
Soups:	Vegetable milk soups or lean meat stock soups
Meats:	Lean meat or fowl, i. e., beef, lamb, veal, liver, chicken or turkey to be broiled, boiled or roasted, not fried; crisply broiled bacon, with fat drained off, on occasion
Fish:	Lean fresh water fish (whitefish, perch, pike, trout or bass, broiled, boiled, poached or baked; shrimp, lobster, or oysters if desired)
Eggs:	One or two daily, soft boiled, poached, shirred or soft scrambled, not fried
Cheese:	Cottage, cream, mild American or mild Swiss
Vegetables:	Three or more servings daily of any type of cooked or raw vegetable with the exception of raw onions, radishes, cucumbers or sauerkraut (at least one serving daily of a raw, green, leafy vegetable)
Potatoes:	Prepared any way except fried
Fruit:	At least three servings daily of any type, canned, stewed or fresh (syrup should be removed from any canned or stewed fruit that is used. At least one serving daily should be of citrus fruit, i. e., 1 orange, ½ grapefruit or the juice of either)
Desserts:	Simple puddings, jello, sponge or pound cake (without icing), vanilla wafers and fruit as specified above
Beverages:	Milk, buttermilk, tea, coffee, cocoa and unsweetened fruit juices
Butter:	As desired.

Foods to Avoid:

	Cakes with icings, sugar, candy, pie, pastry, jelly, honey and syrup; grape and prune juice; alcoholic and carbonated beverages; fat meat and fish, fried foods
Avoid:	Tobacco

Sample Menu

Breakfast	Luncheon	Dinner
Orange juice	Cream of vegetable soup	Tomato juice
Oatmeal	Broiled lake trout	Broiled lamb chops
Poached egg	Chopped spinach	Baked potato, butter
Toast	Fruit salad	Julienne carrots
Butter	Bread	Combination salad with dressing
Coffee	Butter	Bread
No sugar	Baked cup custard	Butter
	Tea or coffee	Baked apple
	No sugar	Tea or coffee
		No sugar

Snacks

10. a. m.: Milk, 6 oz. 3 p. m.: Milk, 6 oz.
Bedtime: Milk, 6 oz.; buttered toast; fruit

Cellu* sugarless sweetener or saccharine may be used instead of sugar

* Registered trade name.

Free sugar in any form was omitted on the basis of the following evidence: 1. The slow injection of dextrose into normal dogs greatly increased their tolerance to subsequent more rapid injection. 2. The deaminization of protein and the formation of carbohydrate in the liver occur slowly, and therefore dextrose will be secreted over a long period and postdigestive hypoglycemia will be delayed if necessary to the next intake of food. However, more frequent feedings than the normal three meals a day were used as an additional factor of safety. A feeding before retiring was added to prevent hypoglycemic manifestations (possibly associated with the "night" pains of peptic ulcer) between the last regular meal at night and the subsequent breakfast. The patient receives his three main meals, a midmorning feeding, one or two midafternoon feedings and a feeding before he retires at night.

Too much emphasis cannot be placed on the importance of a good wholesome breakfast. The menus outlined show the weight which I attach to this observation. Many persons rush to their occupations without being fortified with needed calories to do the day's work. This is especially true of women, who seem proud that they eat little, particularly at breakfast, only to have their efficiency proportionately reduced by limitations of diet. Absenteeism is noteworthy among women workers who go regularly without breakfast. One of the most important functions of food is to give the brain an adequate amount of dextrose at all times. Therefore it may be assumed that a possible vicious circle may exist—first starvation, then altered carbohydrate metabolism due to these stimuli and finally the escape mechanism of fatigue.

Medication.—At the outset it was evident that dietary management alone would not suffice, that drugs which paralyze the parasympathetic nervous system would be needed to prevent emotional stimuli from reaching the pancreas. Clinical experimental studies have shown that atropine will raise the blood sugar level and if continuously given should and probably does maintain a relatively high blood sugar level at all times. No other parasympatholytic drug was found as effective. Therefore, to insure complete atropinization, these patients were given atropine three times a day at meals in doses varying from $\frac{1}{75}$ to $\frac{1}{200}$ grain (1 to 0.3 mg.) and at bedtime from $\frac{1}{100}$ to $\frac{1}{200}$ grain (0.6 to 0.3 mg.). If undue dryness of the mouth or visual disturbance was noted, the dose was reduced. Extreme care was used in giving atropine to elderly patients, because it might precipitate acute glaucoma. For persons with evident eye disease, atropine was distinctly contraindicated. In only 1 case in over 1,200 in which atropine was used for the fatigue or other psychosomatic disturbances was an allergy to the drug noted.

TABLE 3.—*Intravenous Dextrose Tolerance Test Before and After Vagotomy*

	Before Vagotomy	Atropine, 1/50 Grain Hypodermically	After Vagotomy
Fasting	60	83	76
30 min.	100	150	138
60 min.	90	100	122
90 min.	80	85	101
120 min.	72	71	76

As the fatigue improved, the dose of atropine was gradually reduced. Fatigue disappeared under this management. The period of therapy varied from six months to two years. After the cessation of atropine sulfate, intravenous dextrose tolerance tests showed blood sugar levels much higher than the original values; in many patients they resembled those of normal persons. A typical example of the result of combined medical and psychiatric treatment is shown in figure 5.

The dose of atropine was sometimes markedly reduced without the patient's knowledge, and fatigue reappeared. During the early weeks and months of management, if fatigue persisted, the dose of atropine was increased until the fatigue completely disappeared.

The rapidity of improvement of patients placed on this therapeutic regimen was striking. The small group of patients psychiatrically controlled showed an improved psychologic status and a definite reduction

of the period during which psychotherapy was needed. By this regimen the psychiatrist can be aided by the patient's more normal metabolism and his task made definitely easier.

I have been particularly impressed by the good clinical results, with the patient able to lead a more nearly normal existence, the improvement in his emotional state, the return of zest and enthusiasm and the increased efficiency. The possibility of helping out semi-invalided patients is gratifying.

However, a note of warning must be issued. The disappearance of fatigue may stimulate overactivity, and elderly patients must be told to engage in only those activities compatible with their age and the status of their cardiovascular system. This treatment should not be considered a "fountain of youth." The treatment does not attack the cause of the original disturbance, which, once set up, was perpetuated, but it counteracts the pathologic function. Apparently it assists the neurons in dealing with emotional disturbances at a high cortical level, a conclusion attested by the fact that the patients become more susceptible to psychotherapy after dietary and pharmacologic treatment.

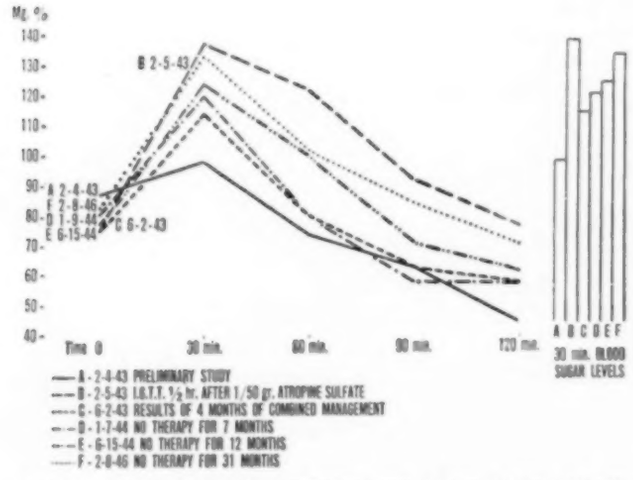

Fig. 5.—Studies of a patient suffering from fatigue before and after medical and psychotherapeutic management. I. G. T. T. (*B*) indicates intravenous dextrose tolerance test.

CONCLUSIONS

1. Life situations and emotions may produce a symptom complex resulting in fatigue.

2. There is experimental and clinical evidence to show that hyperinsulinism is a possible mechanism.

3. The hyperinsulinism may be the result of temporary or prolonged stimulation of the right vagus nerve resulting from emotional processes being relayed through the hypothalamus to the autonomic nervous system.

4. The injection of atropine sulfate prevents this stimulation and allows the blood sugar curves to return to near normal.

5. This hyperinsulinism produces a relative hypoglycemia.

6. A diet low in free sugar has produced definite clinical improvement.

7. Atropine sulfate given orally four times a day probably helps to maintain a higher level of blood sugar at all times and prevents possible fatigue.

8. Patients treated psychotherapeutically and medically could be returned to near normal status.

104 South Michigan Avenue.

Clinical Notes, Suggestions and New Instruments

IDIOSYNCRASY TO AMMONIATED MERCURY

Treatment with 2,3-Dimercaptopropanol (BAL)

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Ammoniated mercury is an effective antiseptic ointment and is therefore widely used. However, standard pediatric textbooks have not described adequately the untoward complications which may arise from the absorption of mercury so applied, and, unless the clinician has had wide experience or is well versed in pediatric or dermatologic literature, so-called calomel disease, which in this case developed from ammoniated mercury, can be baffling.

Because the question [1] whether such an ointment (5 per cent ammoniated mercury) applied to the scalp could give rise to a toxic reaction was asked while this patient was convalescing, we report this case.

In comparable cases reported in the literature by Harper,[2] Bass,[3] Wilbar,[4] Samitz [5] and Fanconi and co-workers [6] the patients recovered without specific therapy. In this instance we believe that without the administration of 2,3-dimercaptopropanol (BAL) the outcome might have been fatal.

REPORT OF A CASE

A 3 year old girl was examined on July 26, 1948 because of several small bald areas on the scalp. The diagnosis of seborrheic dermatitis of the scalp was made, and 3 per cent ammoniated mercury in an ointment base (velvachol) was prescribed. This ointment was applied to the scalp twice daily for three days, at which time a temperature of 103 F. was noted and a diagnosis of acute pharyngitis was made. A triple sulfonamide mixture was prescribed, and the application of ammoniated mercury was discontinued. The patient received three doses of the sulfonamide mixture, each of which was vomited. The fever subsided promptly, and two days later the ammoniated mercury treatment of the scalp and inflamed areas of the forehead was reinstituted. Within forty-eight hours an erythematous rash had developed over the face and body and the fever had recurred.

The patient was examined on August 3. A diagnosis of dermatitis medicamentosa was made, and the ammoniated mercury treatments were discontinued. The patient was reexamined on August 10. The fever had persisted, except when lowered by the administration of acetylsalicylic acid tablets, and the rash was worse. Examination revealed a generalized morbilliform rash and generalized lymphadenopathy, most severe in the postauricular and suboccipital areas. The temperature was 103 F. The red blood cell count was 4,000,000; the hemoglobin was 13 Gm., and the white blood cell count was 5,850, with 39 per cent polymorphonuclear cells, 46 per cent lymphocytes, 3 per cent monocytes and 12 per cent eosinophils. The child had no particular complaint, was still active and had a fair appetite.

The child was admitted to the hospital on August 16 with a temperature of 105 F. Examination revealed the morbilliform rash to be more confluent and violaceous in hue. The

From the Department of Pediatrics, Scott and White Hospital.

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2. Harper, P.: Idiosyncrasy to Ammoniated Mercury Ointment: Report of Two Cases, J. Pediat. **5:** 794 (Dec.) 1934.

3. Bass, M. H.: Idiosyncrasy to Ammoniated Mercury Ointment in Children, Urol. & Cutan. Rev. **45:** 78 (Feb.) 1941.

4. Wilbar, C. L., Jr.: Mercury Poisoning from Topical Application of 15 per Cent Ammoniated Mercury Ointment, J. Pediat. **20:** 89 (Jan.) 1942.

5. Samitz, M. H.: Eczematous Contact Dermatitis Due to Mercurials: Report of a Case of a Reaction to 10 per Cent Ammoniated Mercury Ointment and Associated with Mercurial Poisoning, Arch. Dermat. & Syph. **50:** 10 (July) 1944.

6. Fanconi, G.; Botsztejn, A., and Schenker, P.: Ueber empfindlichkeitsreaktionen auf Quecksilbermedikation im Kindesalter mit besonderer Berücksichtigung der Calomelkrankheit, Helvet paediat. acta (supp. 4) **2:** 3, 1947.

scalp was dry and scaling. The patient was anorexic, listless and irritable. Routine urinalysis revealed no abnormalities. The red blood cell count was 3,520,000, hemoglobin 11.5 Gm. and the white blood cell count 8,000, with 40 per cent polymorphonuclear cells, 33 per cent lymphocytes, 12 per cent monocytes, 1 per cent basophils and 14 per cent eosinophils.

Penicillin, 100,000 units every three hours, was given for forty-eight hours without noticeable effect on the course of the illness. The temperature curve was unremitting at 104 F., except when temporarily lowered with enemas and tepid baths, until specific treatment was begun later. On August 18 the white blood cell count was 4,500, with 6 per cent polymorphonuclear cells, 41 per cent lymphocytes, 30 per cent monocytes and 23 per cent eosinophils. On August 19 there were 30 per cent eosinophils. By August 20, the child's condition suggested clinical acrodynia. She exhibited insomnia and extreme agitation, manifested by wringing and rubbing her hands, scratching her lips and tongue, pulling her hair and beating her head against the crib walls. She was completely anorexic and refused all liquids. Her blood pressure at this time was 100 systolic and 80 diastolic. Spinal fluid examination on August 21 revealed normal conditions. Reactions to heterophil antibody and Weil Felix agglutination tests were negative. Because of the development of multiple paronychia and purulent rhinitis, penicillin, 100,000 units every six hours, was started on August 22. Prompt control of these infections occurred, and penicillin therapy was discontinued on August 25.

In view of the deteriorating state of the patient, in spite of supportive parenteral treatment, a clinical diagnosis of acrodynia due to ammoniated mercury was made on August 23. After collection of a urine specimen for determination of mercury, treatment with BAL, according to the recommendation of Bivings and Lewis,[7] was instituted.

Fig. 1.—*A*, photograph taken at beginning of 2,3-dimercaptopropanol (BAL) administration, August 23. *B*, photograph taken August 31, after BAL therapy.

Figure 1 demonstrates the improvement resultant from specific treatment. The patient began to take nourishment within twenty-four hours and was afebrile within forty-eight hours. BAL therapy was discontinued on the seventh day of treatment because the child complained of transient itching of the hands after each dose. The patient was dismissed on September 1 and was well on October 11, when the residuum of her illness was photographed (fig. 2). On the latter date the white blood cell count was 9,250, with 39 per cent polymorphonuclear cells, 49 per cent lymphocytes, 8 per cent monocytes and 4 per cent eosinophils.

The urinary mercury determinations, obtained by Dr. Warkany through the facilities of the Kettering Laboratories, were reported on October 4. A specimen obtained August 23, before BAL therapy, showed 0.12 mg. of mercury per liter. A specimen obtained September 18, after treatment with BAL, showed 0.02 mg. of mercury per liter. The initial determination revealed, according to Warkany,[8] an appreciable amount of mercury, comparable to that found in cases of acrodynia.

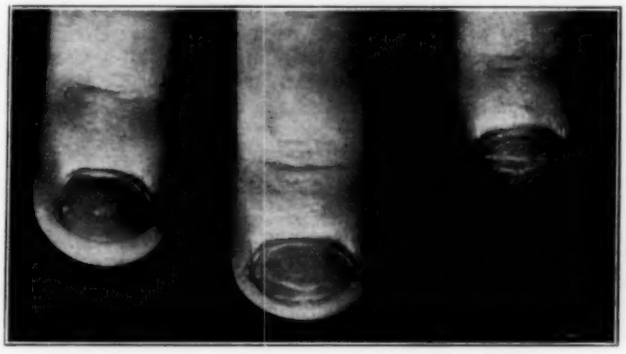

Fig. 2.—Photograph showing disturbance of keratin formation during period of mercury intoxication.

COMMENT

Harper[2] in 1934 reviewed the literature of the past hundred years and found 5 cases of poisoning from the local application of ammoniated mercury. He reported two cases and expressed the opinion that a toxic reaction from local application is more common than the literature would indicate. His first case showed 9 per cent eosinophils on one examination. The course of illness was twenty-four days. The second patient had a course of thirty days. Bass[3] in 1941 reported 5 cases of idiosyncrasy to ammoniated mercury and emphasized the fact that the diagnosis was missed chiefly because the physician was not aware of the clinical picture which such idiosyncrasy may present. Samitz[5] quotes Wise and Sulzberger, who stated, "Millions use these preparations (yellow mercuric oxide and low concentrations of white ammoniated mercury) with impunity, but suddenly some person shows the most devastating, explosive reaction." Fanconi and associates[6] in 1947 reported 56 cases of hypersensitivity reactions to mercury preparations, 39 of which were classified as cases of "calomel" disease (resulting from mild mercurous chloride and santonin used as a vermifuge) and 17 of which were cases of reaction to the external application of mercury. Three of these resembled cases of "calomel" disease.

In view of Fanconi's complete description of this disease, with its rare late complications, such as acrodynia, and the reports of Bivings and Lewis[7] and Elmore,[9] we emphasize the fact that the symptoms in our case were the cardinal symptoms of "calomel" disease, which are: (1) exanthema, (2) fever, (3) generalized glandular swelling, with or without splenic tumor, and (4) eosinophilia. Warkany and Hubbard[10] have led the way toward a definitive diagnosis of mercurial intoxication from whatever source by means of their technic of mercury determination in the urine.

Randall and Seeler[11] have recently published a report on BAL, its history, structure, action and uses. Woody and Kometani[12] have demonstrated its safety in a wide dosage range under circumstances requiring emergency treatment.

7. Bivings, L., and Lewis, G.: Acrodynia: A New Treatment with BAL, J. Pediat. **32**: 63 (Jan.) 1948.

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9. Elmore, S. E.: Ingestion of Mercury as a Probable Cause of Acrodynia and Its Treatment with Dimercaprol (BAL): Report of Two Cases, Pediatrics **1**: 643 (May) 1948.

10. Warkany, J., and Hubbard, D. M.: Mercury in the Urine of Children, Lancet **254**: 829 (May 29) 1948.

11. Randall, R. V., and Seeler, A. O.: BAL, New England J. Med. **239**: 1004 (Dec. 23) and 1040 (Dec. 30) 1948.

12. Woody, N., and Kometani, J.: BAL in the Treatment of Arsenic Ingestion of Children, Pediatrics **1**: 372 (March) 1948.

Russell and co-workers [13] have stated that, in the absence of metallic intoxication, BAL may interfere with magnesium and perhaps calcium metabolism, but this may be ignored if the patient is provided with a high calcium diet, magnesium sulfate and vitamin D.

SUMMARY AND CONCLUSION

A 3 year old girl who exhibited severe idiosyncrasy to ammoniated mercury was treated with 2,3-dimercaptopropanol (BAL) and experienced prompt alleviation of toxic symptoms. Because of this experience it is our opinion that BAL is indicated in the instance of a critically ill patient with a presumptive diagnosis of idiosyncrasy to mercury. However, urine should be obtained for mercury analysis in order to establish a definitive diagnosis.

Council on Foods and Nutrition

This paper was prepared at the request of the Council and is one of a series appearing in THE JOURNAL. *Later the entire series will appear in book form as the Council's Handbook of Nutrition.* JAMES R. WILSON, M.D., *Secretary.*

IRON AND COPPER

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Several recent well documented reviews of iron metabolism are available for those who may be interested in detailed discussions of the subject. Especially to be recommended to the physician are the classical review of Heath and Patek [1] and the discussions by Moore [2] and by Cartwright.[3] Accordingly, this paper will deal specifically with some aspects of iron metabolism which relate directly to an understanding of the clinical syndrome of iron deficiency as encountered in man and its prevention and treatment. This paper is intended to supplement, not to supersede, the excellent discussion of iron in nutrition contained in the first edition of the "Handbook of Nutrition." [4]

The importance of iron deficiency may be illustrated by noting that in the Vanderbilt University Hospital clinics it is the most frequently encountered clinically manifest deficiency disease. It is most often seen in women during the childbearing period and the menopause and in children from 6 months to 2 years of age. The explanation of this distribution will be apparent in the discussion which follows. When encountered in adults the disease is rarely, if ever, of dietary origin and must be regarded as evidence of abnormal blood loss.

METABOLISM OF IRON

The earlier knowledge of iron metabolism was based on studies which employed the usual metabolic balance technic. The past decade has seen the development and widespread application of investigations using radioactive or labeled iron. The principle of this latter type of investigation is simple: the investigator administers the desired quantity (usually quite small and within the physiologic range) of iron, which is tagged by the presence in the sample of varying amounts of one of the radioactive isotopes of iron.[5] Subsequently, at intervals, blood, excreta or tissues are sampled and ashed, and determinations are made of the radioactivity of the iron contained in these substances.[6] One may thereby determine the location of atoms of iron which were administered at the determined time. Up to the instant of decay, radioactive isotopes are physiologically indistinguishable from the ordinary nonradioactive variety. Hence, one may assume that the fate of the radioactive atom is indicative of the fate of all the atoms of iron in the administered sample. Accordingly, a judicious use of quantitative determinations of total iron and radioactivity in such studies permits one to obtain valuable knowledge of the course of iron in metabolism.

Iron exists in foodstuffs in a variety of forms, certain of which are but slightly absorbed. In some instances the poor absorbability of iron is due to the presence of the metal in a sparingly soluble compound or in an organic form from which the iron is poorly liberated. In other instances, the differences in the absorbability of iron, at least in pharmaceutic preparations, are based on differences in valence states of the metal.

It has been held that the availability of iron from a foodstuff could be ascertained by a determination of the amount of iron in the substance which reacted with α,α-dipyridyl. Iron so determined in foodstuffs has often been termed "available iron." There is evidence that some correlation may exist between iron which reacts in this manner and the availability of such iron to rats for hemoglobin synthesis,[7] but similar studies of the relationship in man are lacking. Availability studies of iron compounds carried out on other species, such as rats or dogs, should not serve as more than a tentative basis for conclusions regarding the availability or absorbability of iron by man. This statement is based on the findings of Moore and his co-workers [8] and Hahn and his collaborators,[9] both of whom employed radioactive iron in a study of the relative absorbability by man of ferrous and ferric iron. Both groups of investigators found that ferrous iron was absorbed much more readily by man than was ferric iron. These results were in distinct contrast to similar studies in the dog, which proved that ferric iron is absorbed by this species equally as well as ferrous iron. Obviously, therefore, conclusions based on observations on lower animals are not necessarily valid for man. Investigations of the absorbability or availability of iron products must be verified by studies in man before they serve as a basis for decisions on policies concerning enrichment of foodstuffs with iron. The evidence indicates that iron absorption in the rat and dog is similar. This evidence demonstrates the fallacy inherent in the interpretation of existing evidence for the availability of several iron-containing products which may be used in bread enrich-

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From the Division of Nutrition of the Departments of Medicine and Biochemistry, Vanderbilt University School of Medicine, Nashville.

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3. Cartwright, G. E.: Dietary Factors Concerned in Erythropoiesis, Blood **2**: 111 (March); 256 (May) 1947.

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5. Two radioactive isotopes of iron have been employed: Fe^{59}, with a half-life of forty-seven days, and Fe^{55}, with a half-life of five years. (For a discussion of these technics, see footnotes 6 and 8 and Hevesey, G.: Radioactive Indicators, Their Application in Biochemistry, Animal Physiology, and Pathology, Interscience Publishers, Inc., New York, 1948, p. 556.)

6. (*a*) Hahn, P.: Radioactive Iron Procedures, Indust. & Engin. Chem. **17**: 45 (Jan.) 1945. Balfour, W. M.; Hahn, P. F.; Bale, W. F.; Pommerenke, W. T., and Whipple, G. H.: Radioactive Iron Absorption in Clinical Conditions: Normal, Pregnancy, Anemia, and Hemochromatosis, J. Exper. Med. **76**: 15 (July) 1942. (*b*) Dubach, R.; Moore, C. V., and Minnich, V.: Studies in Iron Transportation and Metabolism, J. Lab. & Clin. Med. **31**: 1201 (Nov.) 1946.

7. Chatfield, C., and Adams, G.: Food Composition, in "Food and Life," Yearbook of Agriculture, Washington, D. C., United States Department of Agriculture, 1939, p. 272.

8. Moore, C. V.; Dubach, R.; Minnich, V., and Roberts, H. K.: Absorption of Ferrous and Ferric Radioactive Iron by Human Subjects and by Dogs, J. Clin. Investigation **23**: 755 (Sept.) 1944.

9. Hahn, P. F.; Jones, E.; Lowe, R. C.; Meneely, G. R., and Peacock, W.: The Relative Absorption and Utilization of Ferrous and Ferric Iron in Anemia as Determined with the Radioactive Isotope, Am. J. Physiol. **143**: 191 (Feb.) 1945.

ment.[10] The use of the dog [11] as an experimental animal for studies on iron availability obviously does not circumvent this fallacy if the data are to be applied to man.

Simultaneously ingested food may decrease iron absorption in man,[12] an effect which may be attributable in part to the effect of bulk.[12] It is reported that certain types of diets may increase the absorption of iron [13] in the rat—an effect which calls to mind the occurrence of ferremia and hemosiderosis in pyridoxine-deficient animals.[14]

The absorption of iron from the gastrointestinal tract is normally a controlled process.[15] In the healthy, nondeficient adult only a small portion of ingested food-iron will be absorbed each day. In an iron-deficient person the absorptive process is much more efficient, and a high percentage of the ingested iron may be taken up. Studies of iron absorption in growing children indicate that the efficiency of the absorption process parallels the need for the element.[16] Similarly, during the latter half of pregnancy the absorptive efficiency is greatly increased,[17] this being the period during which the fetal iron stores are built up.

As indicated, ferrous iron is more efficiently absorbed than ferric iron. The implication of this observation in therapy is obvious. It seems probable that all iron which is absorbed must first be reduced to the ferrous state.[17a] Accordingly, the presence of conditions in the gastrointestinal tract conducive to reducing iron to this state is of importance. Ascorbic acid reduces ferric iron, and there is evidence that it may serve this role under physiologic conditions.

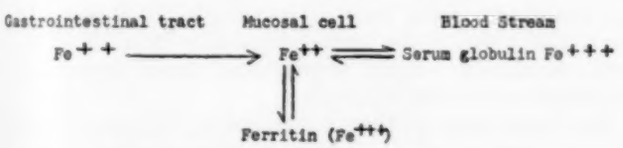

Fig. 1.—Granick's scheme [18] indicating a role of ferritin in absorption of iron.

The control of iron absorption by the intestinal mucosa may be mediated through the iron-containing protein "ferritin." This protein may incorporate up to 23 per cent of iron, which it may readily release. The iron-free protein is called "apoferritin." Ferritin is known to serve as a repository for iron in the body, and Granick [18] has pictured its role in iron absorption, as illustrated by figure 1. This does not appear to be a final picture of the actual mechanism of iron absorption but serves to emphasize the controlled nature of the process and a probable role of ferritin in it.

Absorbed iron is transported in the plasma in the ferric state as one of the globulin fractions.[19] The quantitative determination of serum iron is of such value that it warrants more widespread use in this country. A recently described microprocedure [20] should extend the range of usefulness of the measure. The normal range of values for serum iron is usually stated to be 80 to 180 micrograms per hundred millimeters. Low values are encountered in the hypochromic microcytic anemia of iron deficiency and in the anemia of infection. Higher than normal values are met in pernicious anemia and, possibly, in the other macrocytic anemias, although the evidence on some of these latter is insufficient to permit a categorical statement.

TABLE 1.—*Iron Requirements for Growth (Males)**

Year of Life	Total Annual Requirement of Iron (Gm.)
1	0.195
2	0.112
3	0.080
4	0.092
5	0.098
6	0.079
7	0.080
8	0.070
9	0.072
10	0.152
11	0.130
12	0.137
13	0.189
14	0.198
15	0.314
16	0.313
17	0.353
18	0.183
19	0.149
20	0.081
21	0.071
22	0
23	0
Total requirement: birth to 21 years	3.148

* From Heath and Patek.[1]

Iron which is given intravenously disappears from the plasma until a level of between 300 and 400 micrograms per hundred millimeters is established. The measure of the concentration of iron which can be retained by the plasma under such circumstances is spoken of as the iron-binding capacity of the serum. Cartwright [21] has shown that the hypoferremia of chronic infections is accompanied by a decrease in the iron-binding capacity of the serum and that this latter may be increased by administration of a globulin fraction.

Iron is stored in the tissues, most likely in a number of compounds. The storage iron appears to exist in two parts: (1) a readily available "labile iron pool," [22] which is made up of recently absorbed iron plus that recently released during the breakdown of hemoglobin.

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22. Greenberg, G. R., and Wintrobe, M. M.: A Labile Iron Pool, J. Biol. Chem. **165:** 397 (Sept.) 1946.

and (2) a more fixed, less readily available, tissue iron. The chief sites of storage iron are liver, spleen, bone marrow and kidneys.

In addition to storage iron, the tissues contain so-called "parenchymal iron," which is the relatively fixed iron present in muscle and other tissues and not contained in muscle hemoglobin. Parenchymal iron is held in the iron-containing enzymes such as cytochrome, catalase, peroxidase and related compounds. Parenchymal iron and muscle hemoglobin have been termed by Hahn [23] as "inviolate stores of iron which are not drawn on no matter how great the emergency due to anemia."

TABLE 2.—*Iron Requirements for Growth, Menstruation and Pregnancy* *

Year of Life	Total Annual Requirement of Iron (Gm.)
1	0.182
2	0.112
3	0.092
4	0.080
5	0.087
6	0.106
7	0.078
8	0.067
9	0.108
10	0.120
11	0.163
12	0.164
13	0.192
14	0.145
15	0.468
16	0.424
17	0.498
18	0.435
19	0.452
20	0.365
21	0.358
22	0.298
23	0.298
24	0.298
25	0.374 †
26	0.298
Total requirement: birth to 47 years	12.222

* From Heath and Patek.[1]
† Calculated for pregnancy.

The body has a minimal capacity for losing iron except through blood loss.[13] Practically no iron is excreted in the urine, and the excretory iron in the feces comprises less than 1.0 mg. per day.[24] Moore [25] has failed to confirm the claim of Mitchell and Hamilton [26] that a large loss of iron occurs through the perspiration.

REQUIREMENTS FOR IRON

The calculations of iron requirements which were made by Heath and Patek [1] are probably as valid as any which could be made today. These estimates, which are summarized in tables 1 and 2, indicate that the times of the greatest requirement for iron, both relatively and absolutely, are during the first two years of life and the rapid growth of adolescence and, in women, throughout the childbearing period. After growth ceases in the man, the requirement for iron falls to an exceedingly low level. For women the requirement remains higher because of the loss of iron in menstrual blood and the process of reproduction. After the menopause the requirement drops. These requirements were calculated from estimates of the iron needed to build body tissue and to replace body losses. They are not estimates of dietary requirements. The Food and Nutrition Board of the National Research Council has given estimates of allowances of iron in the diet in order to provide an abundantly adequate supply of dietary iron. The figures from the 1948 revision are reproduced in table 3. Somewhere between these two estimates probably lies the true minimal dietary requirement of the metal.

I feel that it will remain futile to attempt to set a single figure as the requirement for iron in the diet. The physiologic availability of iron varies from foodstuff to foodstuff and is dependent on the composition of the remainder of the diet. For all nutrients there exist important physiologic variations in requirements from person to person. Accordingly, any single figure for requirements must remain a mere approximation.

At this point, it may be well to consider terminology concerning physiologic availability of iron. It has been pointed out that the term "available iron" has been used in connection with a chemical procedure which does not necessarily measure the iron which can be absorbed and utilized by man. It appears to be mandatory that iron is in the ferrous state at the moment of absorption by man. Therefore, all the iron which is absorbed from the human intestine would seem to enter the body with the same potentialities for utilization, regardless of the original form of the iron. Accordingly, it appears to me that the use of the term "absorbable iron" in foodstuffs would be a more precise and useful term than "utilizable or available iron."

The total iron content, expressed in milligrams per hundred grams, of the edible portion of some representative foods are listed in table 4. The values given in this table permit the following generalizations. Relatively rich sources of iron are organ meats (heart and liver), egg yolk, dried legumes, oatmeal and cane molasses. Poor sources of iron include milk and milk products, fats and oils, fruits and root vegetables, unenriched white flour, granulated sugar and degerminated cornmeal. Foods of intermediate iron content include muscle meats, fish, poultry, nuts, green and green leafy vegetables, enriched flour and whole grain meal.

TABLE 3.—*Recommended Daily Dietary Allowances*

	Iron (Mg.)
Man (154 lb., 70 Kg.)	
Sedentary	12 *
Physically active	12 *
With heavy work	12 *
Woman (123 lb., 56 Kg.)	
Sedentary	12
Moderately active	12
Very active	12
Pregnancy (latter half)	15
Lactation	15
Children up to 12 years	
Under 1	6
1-3 (27 lb., 12 Kg.)	7
4-6 (42 lb., 19 Kg.)	8
7-9 (58 lb., 26 Kg.)	10
10-12 (78 lb., 35 Kg.)	12
Children over 12 years	
Girls, 13-15 (108 lb., 49 Kg.)	15
16-20 (122 lb., 55 Kg.)	15
Boys, 13-15 (108 lb., 49 Kg.)	15
16-20 (141 lb., 64 Kg.)	15

* There is evidence that the male adult needs relatively little iron. The need will usually be provided for if the diet is satisfactory in other respects.

23. Hahn, P. F.: The Metabolism of Iron, Medicine **16**: 249 (Sept.) 1937.
24. Moore, C. V.: Estimated from data of Dubach, Moore, and Minnich [9b] on Excretion of Intravenously Injected Iron in Patients with Hemolytic Anemia.
25. Moore, C. V.: Iron Metabolism and Hypochromic Anemia, paper presented at Symposium: Currents in Nutrition, University of Illinois College of Medicine, Chicago, November 19, 1949.
26. Mitchell, H. H., and Hamilton, T. S.: The Dermal Excretion under Controlled Environmental Conditions of Nitrogen and Minerals in Human Subjects, with Particular Reference to Calcium and Iron, J. Biol. Chem. **178**: 345 (March) 1949.

IRON DEFICIENCY

The pathogenesis of iron deficiency is usually predictable from the age of the person. In the infant iron deficiency is most often of dietary origin. In the adult the deficiency is conditioned by chronic blood loss.

TABLE 4.—*Iron Content of Selected Foods* *

Food Item	Iron (Mg./100 Gm.) †
Milk	
Evaporated, unsweetened	.17
Fresh whole	.07
Ice cream, plain	.10
Cheese: Cheddar type	.57
Bacon, medium fat	.8
Butter	.2
Lard, other shortening	0
Egg yolk, fresh	7.2
Eggs, whole, fresh	2.7
Beef	
Roasting meat	2.8
Round steak (wholesale round)	2.9
Pork: Ham, smoked	2.5
Variety meats, meat mixtures	
Heart, fresh	6.2
Liver, fresh	12.1
Poultry: chicken, roasters	1.9
Fish, miscellaneous, medium fat	1.9
Dry Beans and Peas, Nuts	
Cowpeas	7.8
Peanuts, roasted	1.9
Vegetables, Fresh	
Beans, lima, green	2.3
Beets	1.0
Broccoli	1.3
Carrots	.8
Kale	2.2
Lettuce, headed	.5
Mustard greens	2.9
Potatoes	.7
Spinach	3.0
Turnip greens	2.4
Turnips	.5
Fruit, Fresh	
Apples	.3
Apricots	.5
Cantaloups	.4
Grapefruit	.3
Oranges	.4
Corn meal	
White, degerminated	1.0
White, whole grain	2.7
Flour	
Wheat, patent	.7
Wheat, patent, enriched	2.9
Whole wheat	3.8
Bread	
White, enriched	1.8
Whole wheat	2.6
Cereals	
Oatmeal	5.2
Rice flakes; puffed rice	.9
Sugars, Sweets	
Honey	.9
Molasses, cane	6.7
Sugar, brown	2.6
Sugar, granulated or powdered	.1
Yeast, dried, brewer's	18.2

* From the United States Department of Agriculture, Miscellaneous Publication No. 572. † Edible portion.

The fetal stores of iron are deposited during the last trimester of pregnancy. Although the interpretation has been questioned, there is considerable evidence to indicate that fetal stores of iron at birth may be considerably influenced by the nutrition of the mother relative to iron during pregnancy.[27] Thus, Strauss [28] found that infants born to mothers who were anemic during pregnancy had a high incidence of iron deficiency anemia during the first year of life. The iron stores of premature infants are less than those of full term infants. At birth a considerable amount of iron is contained in the infant's body because of the plethora of red cells and hemoglobin. Normally, the iron available from the breakdown of the excessive hemoglobin and from normal stores will be sufficient to carry the infant through the first few months of life on the low iron intake provided by milk. From approximately 6 months of age on, however, the body stores of iron may be insufficient to meet the demands of the growing infant, and unless an intake of iron other than that contained in milk is provided, the hypochromic microcytic anemia of iron deficiency may appear. This manifestation of iron deficiency is most frequently encountered in children from 6 months to 2½ years of age who have received a diet based on cow's milk formula. From table 4 it is apparent that the provision of orange juice as an antiscorbutic and vitamins A and D in a fish oil would not suffice to protect the infant against the development of iron deficiency. This illustrates the desirability of a variety of foods in the infant's diet.

The clinical evidence indicates that by the time adulthood is reached even the poorest dietary regimens which are likely to be encountered in this country are sufficient to prevent iron deficiency in the absence of chronic blood loss. Iron deficiency does not often occur as a result of a single massive hemorrhage. Instead, it results from repeated losses of blood. The most common sources of these losses are: menorrhagia, functional or due to fibroids; bleeding peptic ulcers; hemorrhoids; menopausal menorrhagia; abortion, miscarriage or bleeding after delivery; parasitic infestation, especially with hookworm, and blood loss secondary to malignant changes either of the gastrointestinal tract, nasopharynx or genitourinary tract. Less frequently one finds that the fault lies in chronic pulmonary hemorrhage, renal hemorrhage (tuberculosis or hypernephroma) and blood losses from ulcerative colitis, rectal polyps or even diaphragmatic hernia.

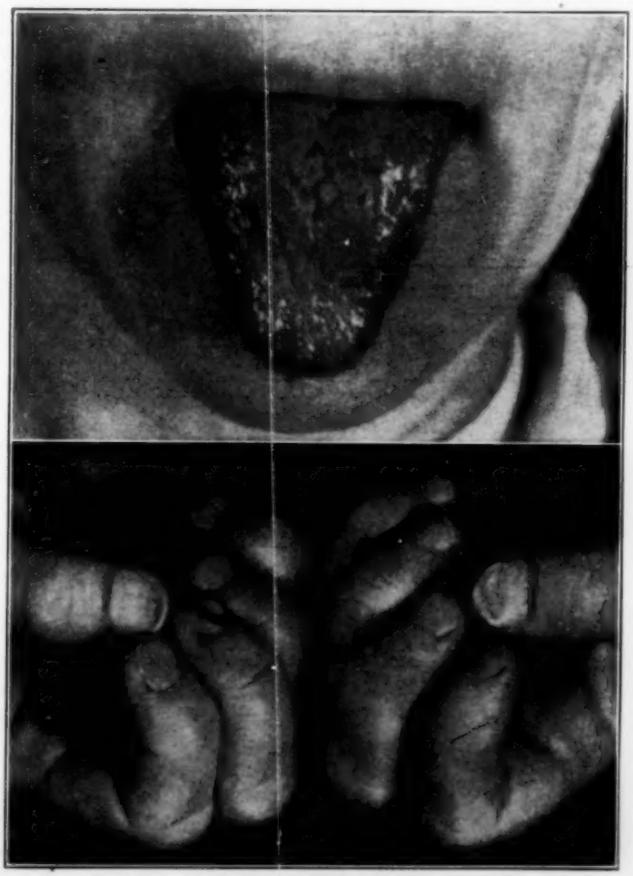

Fig. 2.—Glossitis, angular stomatitis and koilonychia encountered in a patient with hypochromic microcytic anemia due to menorrhagia. These lesions, as well as the anemia, responded to therapy with ferrous sulfate alone.

27. Guest, G. M.: Hypoferric Anemia in Infancy. Symposia on Nutrition: I. Nutritional Anemia, Cincinnati, The Robert Gould Research Foundation, Inc., 1947, p. 144.

28. Strauss, M. B.: Anemia of Infancy from Maternal Iron Deficiency in Pregnancy, J. Clin. Investigation **12**: 345 (March) 1933.

Peculiarly enough, the pathology of iron deficiency has not been described in detail.[29] The iron-deficient person usually is rather nervous, easily fatigued and listless; palpitation on exertion, a sore tongue, angular stomatitis and dysphagia may be present. A hypochromic microcytic anemia is invariably seen. When all these conditions are present, the syndrome is referred to as the Plummer-Vinson syndrome. Koilonychia may also be seen. Any combination of these conditions may be encountered.[30] Signs other than the anemia are not usually encountered in children. The oral lesions and nail changes are illustrated in figure 2. The oral lesions occur in one degree or another in about 10 per cent of iron-deficient adults, in my experience. Koilonychia is less frequently met.

The anemia of iron deficiency is hypochromic microcytic anemia and is accompanied by normoblastic hyperplasia of the bone marrow. Plasma iron levels are low in this type of anemia, and iron absorption curves do not show a rise after an oral test dose. Iron absorption, however, is increased, as one can demonstrate by use of the radioactive iron technic.

A discussion of anemia such as this raises the question of when a person or a population should be considered anemic. The usual arbitrary figures for "normal" hemoglobin and red blood cell values give no indication of the variability to be expected in a healthy population. Several modern studies of hemoglobin levels in population groups other than hospital groups indicate something of this variability. Figure 3, for example, illustrates the variation in average hemoglobin levels which were encountered in different physiologic groups within populations in Great Britain.[31] Table 5 indicates the variability in hemoglobin levels observed in a study of 3,029 persons in North Carolina.[32] Like variations have been observed in other similar studies. It is to be noted that the lower limits of the nineteen-twentieths of the distributions in the North Carolina studies are approximately 11 Gm. for children under 12 years of age, approximately 11.5 Gm. for white women and approximately 12 Gm. for white men. In each case, the values for the Negro groups are from 0.2 to 0.5 Gm. less. These lower limits represent a useful statistical division for those values likely to be associated with abnormality. It is recognized that such average hemoglobin values do not necessarily indicate the level conducive to the best health. Nevertheless, such observations among a non-ill population do caution against the designation of a large group of the population as anemic or iron-deficient[33] merely because they fall below some arbitrary hemoglobin levels, especially in view of the clinical evidence that many of these persons cannot have their hemoglobin levels increased by the administration of iron.[34]

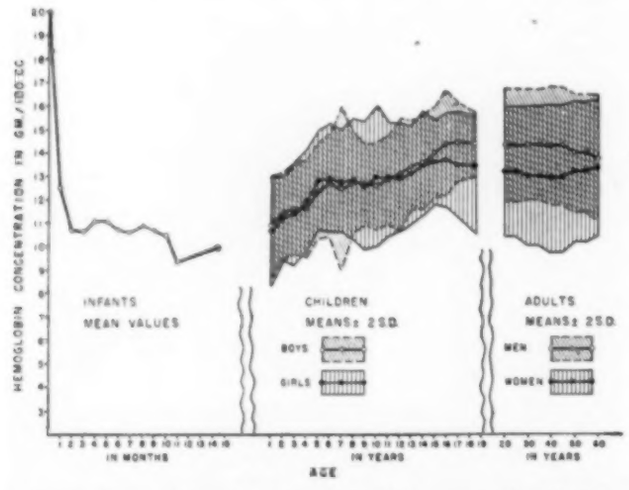

Fig. 3.—The variations in average hemoglobin concentrations throughout the life span are shown. This chart of mean hemoglobin concentration in grams per hundred cubic centimeters at various ages was constructed by accepting the value of 13.8 Gm. per hundred cubic centimeters as 100 per cent (Haldane). The limits of plus or minus 2 standard deviations are such that one may expect them to include approximately 95 per cent of the values encountered in healthy persons. Of particular interest are (1) the wide swings in hemoglobin level which occur between birth and adulthood, (2) the separation of means for boys and girls at puberty, with the subsequent decrease in the sex differences after 40 years of age and (3) the greater variation in values for women than for men—a phenomenon more apparent at the menopause. (Constructed from data of the Medical Research Council, Special Report Series no. 252.[31])

TABLE 5.—*Distribution Constants of Hemoglobin Levels for White and Negro Populations (North Carolina)*[32]

	White, Hemoglobin (Gm./100 Cc.)	Negro, Hemoglobin (Gm./100 Cc.)
Mean:		
Under 12		
Boys	12.67 ± 0.046	11.89 ± 0.078
Girls	12.54 ± 0.046	12.13 ± 0.062
12 and over		
Men	14.25 ± 0.049	13.76 ± 0.086
Women	12.87 ± 0.043	12.16 ± 0.087
Women (fitted curve)	13.08	12.64
Limits of nineteen-twentieths of distribution:		
Under 12		
Boys	10.97 — 14.37	9.77 — 14.01
Girls	10.95 — 14.17	10.47 — 13.79
12 and over		
Men	11.88 — 16.62	11.31 — 16.21
Women	10.41 — 15.33	9.36 — 14.96
Women (fitted curve)	11.30 — 14.88	11.04 — 14.24

The finding of a low hemoglobin level is not alone sufficient for the diagnosis of iron deficiency anemia, whether in a particular person or a population group. Unfortunately, estimates of the prevalence of iron deficiency have sometimes been based on this single criterion.[33] The simultaneous determination of hemoglobin concentration, red blood cell counts (RBC) and of packed cell volume (PCV) permits the calculation of exceedingly useful volume and concentration indexes. These indexes are as follows:

$$\text{Mean corpuscular volume (MCV) in cubic microns} = \frac{\text{Volume of packed red cells (PCV), cc. per 100 cc.} \times 10}{\text{Red cell count (RBC), million per cu. mm.}}$$

$$\text{Mean corpuscular hemoglobin (MCH) in micromicrograms} = \frac{\text{Hemoglobin, Gm. per 100 cc.} \times 10}{\text{Red cell count (RBC), million per cu. mm.}}$$

$$\text{Mean corpuscular hemoglobin concentration (MCHC) in per cent} = \frac{\text{Hemoglobin, Gm. per 100 cc.} \times 100}{\text{Volume packed red cells (PCV), cc. per 100 cc.}}$$

29. Follis, R. H., Jr.: The Pathology of Nutritional Disease, Springfield, Ill., Charles C Thomas, Publisher, 1948.

30. Heath and Patek.[1] Darby, W. J.: The Oral Manifestations of Iron Deficiency, J. A. M. A. **130**: 830 (March 30) 1946. Waldenström, J.: Iron and Epithelium: Some Clinical Observations, Acta med. Scandinav. 1938, supp. 90, p. 380.

31. Haemoglobin Levels in Great Britain in 1943 (with Observations upon Serum Protein Levels), Committee on Haemoglobin Surveys, Medical Research Council, Special Report Series, no. 252, London, His Majesty's Stationery Office, 1945.

32. Milam, D. F., and Muench, H.: Hemoglobin Levels in Specific Race, Age, and Sex Groups of a Normal North Carolina Population, J. Lab. & Clin. Med. **31**: 878 (Aug.) 1946.

33. Committee on Diagnosis and Pathology of Nutritional Deficiencies, Food and Nutrition Board: Inadequate Diets and Nutritional Deficiencies in the United States: Their Prevalence and Significance, New York, Bulletin of the National Research Council, no. 109, 1943.

34. Fowler, W. M., and Barer, A. P.: Some Effects of Iron on Hemoglobin Formation, Am. J. M. Sc. **201**: 642 (May) 1941.

The usefulness of these indexes in the classification of anemias is indicated by table 6, which has been adopted from the report by Wintrobe.[35]

In addition to these specific characteristics of iron deficiency anemia, one may encounter the several manifestations of the anemic state. In particular, one may observe cardiac abnormalities [36] such as hemic murmurs, cardiac enlargement, symptoms of angina pectoris, palpitation and even electrocardiographic changes. Dyspnea and edema are not infrequently observed.

The anemia of iron deficiency is most likely to be confused with anemias of infection, hemolytic anemias and, occasionally, myelophthisic anemias. In animals, there are other types of microcytic anemia, such as that due to pyridoxine deficiency or to cobalt deficiency. The analogues of these, however, have not been identified in man.

PREVENTION AND THERAPY OF IRON DEFICIENCY

The prevention of iron deficiency anemias in infants consists of proper attention to the nutritional state of the mother during pregnancy and the early introduction of a variety of foodstuffs in the diet of the baby. It might be noted that breast milk is slightly richer in iron than cow's milk and, accordingly, breast feeding of the infant may be of aid in the prevention of the development of iron deficiency. Once iron deficiency has developed, therapy with a suitable preparation of a ferrous salt, plus correction of the diet, should result in a rapid recovery.

The prevention of iron deficiency in the adult resides in the early recognition and correction of sources of chronic blood loss and, in addition, that which may be called "preventive therapy" or supplementation for those persons with conditions previously enumerated which impose the stress of excessive loss of iron in blood or during the latter part of pregnancy. It is logical to reason that increasing the dietary intake of iron above the present level can be expected to have little influence on the prevalence of iron deficiency within the adult population.

The treatment of iron deficiency in the adult consists of detection of the source of blood loss and correction of the defect and the oral administration of a readily absorbed preparation of iron, preferably ferrous sulfate. The simple preparations of ferrous sulfate are equally as effective as any combination of iron with yeast, liver, folic acid or other minerals. Iron is effective only in the treatment of iron deficiency anemia. It has no value in the treatment of the anemia of infection, of pernicious anemia, sprue or other types of anemia unless they are accompanied by an associated iron deficiency. Specific therapy is followed by moderate reticulocytosis and a gradual rise of hemoglobin level at a rate of 0.1 to 0.2 Gm. per hundred milliliters per day. The cell volume increases and the hematologic picture returns to normal. Figure 4 illustrates the response of a patient treated with 0.3 Gm. of ferrous sulfate daily.

In view of the considerations which have been reviewed, it is not possible to evaluate the benefits of including iron in the enrichment of flour and bread. As a matter of fact, the evidence is unconvincing that certain of the iron preparations which have been used in enrichment mixtures actually result in an increase in the amount of absorbable iron in the diet. The importance of the problem of iron deficiency is such that a solid appraisal of the program based on human physiology is needed.

TABLE 6.—*Classification of Principal Anemias (Modified after Wintrobe [35])*

Anemias	MCV (Cu. μ)	MCHC (%)	Syndrome	Characterized by:	Responds to:
Hypochromic microcytic	< 80	< 30	A. Iron deficiency anemias of all sorts—including dietary deficiency, excessive blood loss, hookworm infestation and repeated pregnancies.	Low serum iron; normoblastic marrow	Iron and correction of blood loss
Simple microcytic	< 80	> 30	Subacute and chronic inflammatory diseases	Low serum iron; hypercupremia	Treatment of cause
Normocytic	80-94	> 30	A. Myelophthisic and aplastic anemias; chronic disease	.....	Transfusion and treatment of cause
			B. "Physiologic" anemia (hydremia) of pregnancy		
Macrocytic	> 94	> 30	A. Pernicious anemia; Sprue; Pernicious anemia of pregnancy; Macrocytic anemia of celiac disease; Nutritional macrocytic anemia; Tropical macrocytic anemia; Macrocytic anemia associated with conditions such as carcinoma of stomach and liver disease	Megaloblastic marrow; high or normal serum iron	Liver extract, folic acid, vitamin B_{12} or animal protein factor
			B. Conditions usually associated with normocytic anemias	.....	Transfusions and treatment of causes

TOXICITY OF IRON

There exists an exceedingly wide range of safety between the therapeutic and toxic doses of orally administered iron. While even ordinary therapeutic doses of soluble iron preparations may produce some gastrointestinal symptoms, these are seldom of much importance. Massive overdosage of iron, however, may produce serious, even fatal, consequences. Thus, the ingestion by children of amounts of ferrous sulfate of 6.0 to 10.0 Gm. has produced death with acute hemorrhagic gastritis and liver damage.[37] Ingestion by a 2 year old child of 2.0 Gm. of ferrous sulfate resulted in a severe, but not fatal, gastritis. Obviously, therapeutic iron preparations should be kept out of the reach of small children. From a pharmacologic study of iron

35. Wintrobe, M. M.: Anemia: Classification and Treatment on the Basis of Differences in the Average Volume and Hemoglobin Content of the Red Corpuscles, Arch. Int. Med. **54**: 256 (Aug.) 1934.

36. (*a*) Hunter, A.: The Heart in Anaemia, Quart. J. Med. **15**: 107 (April) 1946. (*b*) Wintrobe, M. M.: The Cardiovascular System in Anemia, Blood **1**: 121 (March) 1946.

37. Forbes, G.: Poisoning with a Preparation of Iron, Copper, and Manganese, Brit. M. J. **1**: 367 (March 22) 1947.

preparations, Somers [38] has estimated the lethal dose for an adult as at least several hundred 0.2 Gm. tablets of ferrous sulfate.

The parenteral administration of even small amounts of iron (colloidal ferric oxide or colloidal ferric hydroxide) has been termed [39] "impractical, dangerous, and unnecessary as a therapeutic measure." It is followed by a febrile reaction, shock and thrombosis of the receiving vein. The toxic symptoms have been described in detail by Goetsch, Moore and Minnich.[39] Nissim,[40] however, has reported on a preparation of "saccharated iron" which it seems may be administered to patients intravenously in quantities supplying up to 500 mg. of elemental iron without these toxic reactions developing. Further development of such preparations may offer feasible parenteral therapy for limited use.

COPPER

Any attempt to arrive at a conclusive statement regarding the occurrence of copper deficiency in man or the human requirements of copper would be most

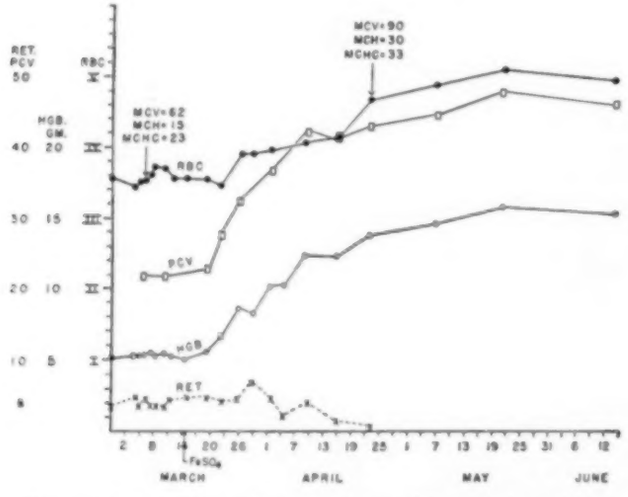

Fig. 4.—Response of a patient with iron deficiency (microcytic hypochromic anemia) to ferrous sulfate administered in oral doses of 0.3 Gm. daily, beginning on the date indicated by the arrow.

premature and would, therefore, be controversial. Most of the clinical studies [41] on man which purport to produce evidence of copper deficiency are open to definite criticism. Rigidly designed studies on man in this area are badly needed.

Certain facts relative to the nutritional role of copper seem indisputable. Copper is an essential nutrient for rats and for several other experimental animals. A deficiency of the element is manifest by a hypochromic, usually microcytic, anemia and general debility as well as depigmentation. There occurs a decrease in the activities of oxidative enzymes (cytochrome, cytochrome oxidase and catalase) in the tissues of deficient rats. Herbivora are particularly susceptible to this deficiency, and it may occur under practical feeding conditions, especially if a pasture area low in copper has been treated with molybdenum.[42] The anemia of copper deficiency is a reflection of the inability to mobilize iron for hemoglobin production.

The human diet ordinarily contains 2 to 4 mg. of copper per day. The metal may be absorbed from the gastrointestinal tract with retention of some 5 to 40 per cent of the intake. Balance studies on man reveal that a daily intake of approximately 2.0 mg. will maintain adults in balance. Such evidence, however, should not be construed as defining a requirement. The copper content of whole blood is approximately equally divided between cells and plasma and usually lies between 90 and 150 micrograms per hundred milliliters for men and 100 and 160 micrograms for women. Similar levels are obtained for serum copper—thus, Nielsen [43] reports 110 plus or minus 12 micrograms per hundred milliliters for healthy men and 123 plus or minus 16 micrograms for healthy women. He noted appreciable diurnal variations in the serum copper values. During the latter half of pregnancy there is a definite rise in the copper content of the serum, a rise which disappears within one to two months after delivery. Serum copper values are low (by adult standards) in the newborn. Van Ravesteyn [44] found that giving copper by mouth did not appreciably increase the serum level or the urinary content of the element. This latter varied from 0 to 12.5 micrograms per hundred milliliters. The administration of copper intravenously resulted in a transitory rise in serum and urinary content, but both returned to pretreatment levels within a few hours. Biliary and fecal content of copper rose sharply after administration of copper by either oral or intravenous routes. It is apparent that copper is excreted by man in the bile, and there is a possibility that it is excreted in part by the intestinal wall.

Milk is extremely low in copper content. The successful production of copper deficiency in rats fed a milk diet has led to the repeated suggestions that infants restricted to milk alone may reveal signs of copper deficiency and that copper is a logical adjunct to iron for therapy of hypochromic microcytic anemia of infants. While the evidence indicates that some hemopoietic effect of copper may have been observed in an occasional anemic infant, there is need for a definitive study of this claim. The point is one which has more practical bearing on the prevention of this anemia than on its treatment, for most infants with hypochromic microcytic anemia respond satisfactorily to the iron preparations in common use.

In the adult, hypochromic microcytic anemia is due to blood loss, hence it would not be expected that copper deficiency would be encountered. The investigations of the hemopoietic effect of copper leave me unconvinced that copper deficiency has been encountered in the adult.

38. Somers, G. F.: Relative Oral Toxicity of Some Therapeutic Iron Preparations, Brit. M. J. **2**: 201 (Aug. 9) 1947.

39. Goetsch, A. T.; Moore, C. V., and Minnich, V.: Observations on the Effect of Massive Doses of Iron Given Intravenously to Patients with Hypochromic Anemia, Blood **1**: 129 (March) 1946. Heath, C. W.; Strauss, M. B., and Castle, W. B.: Quantitative Aspects of Iron Deficiency in Hypochromic Anemia, J. Clin. Investigation **11**: 1293 (Nov.) 1932.

40. Nissim, J. A.: Intravenous Administration of Iron, Lancet **2**: 49 (July 12) 1947.

41. The literature on copper metabolism and deficiency is well summarized in the following reviews: Schultze, M. O.: Metallic Elements and Blood Formation, Physiol. Rev. **20**: 37 (Jan.) 1940. Schultze, M. O.: Some Biochemical Aspects of Metabolism of Iron and Copper, Symposia on Nutrition: I. Nutritional Anemia, Cincinnati, The Robert Gould Research Foundation, Inc., 1947, p. 99. Cartwright,[3] Anonymous: Present Knowledge of Iron and Copper in Human Nutrition, Nutrition Rev. **4**: 291 (Oct.) 1946.

42. Davis, G. K.: Mineral Element Deficiencies and Their Influence on the Growth and Nutrition of Animals, Proceedings of the Southern Conference on Nutrition and Public Health, School of Public Health, Chapel Hill, University of North Carolina, Nov. 14-15, 1947, p. 9.

43. Nielsen, A. L.: On Serum Copper: I. Introduction, Acta med. Scandinav. **118**: 84 (Sept.) 1944; III. Normal Values, ibid. **118**: 87 (Sept.) 1944; IV. Pregnancy and Parturition, ibid. **118**: 92 (Sept.) 1944.

44. Van Ravesteyn, A. H.: Metabolism of Copper in Man, Acta med. Scandinav. **118**: 163. (Sept.) 1944.

A disease of ruminants known as scouring has long been associated with "teart" pasture areas. The herbage from these areas has been found unusually high in content of molybdenum.[45] The condition is counteracted by the feeding of copper or by the addition of copper to the soil. This antagonism of molybdenum and copper in animal nutrition raises the question of a possibly toxic effect of certain of the pharmaceutic preparations of iron with molybdenum which are now marketed and used in prenatal care.[46] This question becomes the more pertinent when it is recalled that there normally occurs a pronounced rise in serum copper in pregnancy and that the fetal (cord) serum is low in copper. Will administered molybdenum upset an important metabolic adjustment in copper metabolism? I have been unable to find evidence bearing on this point.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

METHAMPHETAMINE HYDROCHLORIDE (See New and Nonofficial Remedies 1949, page 227).

The following dosage form has been accepted:

MCNEIL LABORATORIES INC., PHILADELPHIA 32

Elixir Syndrox Hydrochloride: 473 cc. and 3.78 liter bottles: An elixir containing .67 mg. of methamphetamine hydrochloride in each cc.

PENICILLIN FOR ORAL ADMINISTRATION (See New and Nonofficial Remedies 1949, page 156).

The following dosage form has been accepted:

THE BIO-RAMO DRUG CO., BALTIMORE 1

Tablets Crystalline Sodium Penicillin G (*Buffered*): 50,000 and 100,000 units. Buffered with sodium benzoate.

SULFADIAZINE-SULFAMERAZINE COMBINED (See THE JOURNAL, May 7, 1949, page 21).

The following dosage form has been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Dulcet Tablets Duozine: 0.15 Gm. Each tablet contains 75 mg. of sulfadiazine and 75 mg. of sulfamerazine.

U. S. trademark 301,662 (Dulcet).

SULFADIAZINE-SULFAMERAZINE-SULFAMETHAZINE MIXTURE (See THE JOURNAL, Dec. 24, 1949, page 1233).

The following dosage form has been accepted:

MARVIN R. THOMPSON, INC., STAMFORD, CONN.

Suspension Sulfa-tri-azine with Sodium Lactate: 473 cc. bottles: A suspension containing 33 mg. each of sulfadiazine, sulfamerazine and sulfamethazine and 0.3 Gm. of sodium lactate in each cc.

U. S. patent 2,460,437.

THROMBIN, TOPICAL (See New and Nonofficial Remedies 1949, page 354).

The following dosage form has been accepted:

CUTTER LABORATORIES, BERKELEY 1, CALIF.

Thrombin (Human): 2,500 and 5,000 units sterile dried thrombin (human) each packaged with 2.5 cc. and 10 cc. vial of isotonic sodium chloride solution, respectively.

Licensed under U. S. patent 2,389,074.

45. Stiles, W.: Trace Elements in Plants and Animals, 1946, New York, The Macmillan Company, especially pp. 131-135.

46. Neary, E. R.: The Use of Molybdenized Ferrous Sulfate in the Treatment of True Iron Deficiency Anemia of Pregnancy, Am. J. M. Sc. 212:76 (July) 1946.

TETANUS TOXOID-U.S.P. (See New and Nonofficial Remedies 1949, p. 501).

The following dosage form has been accepted:

CUTTER LABORATORIES, BERKELEY 1, CALIF.

Tetanus Toxoid: 1.5 cc. vials (one immunization) and 15 cc. vials (ten immunizations). Preserved with thimerosal 1:10,000.

CITRATED NORMAL HUMAN PLASMA-U.S.P. (See New and Nonofficial Remedies 1949, p. 474).

The following dosage form has been accepted:

CUTTER LABORATORIES, BERKELEY 1, CALIF.

Normal Human Plasma (Dried): Equivalent to 250 cc. restored plasma, packaged with 250 cc. of 0.1 per cent citric acid in distilled water as diluent.

DIHYDROXY ALUMINUM AMINOACETATE (See New and Nonofficial Remedies 1949, p. 336).

The following dosage form has been accepted:

THE E. L. PATCH COMPANY, BOSTON.

Magma Alzinox: 250 cc. bottles: A suspension containing 0.1 Gm. of dihydroxy aluminum aminoacetate in each cc. Preserved with 0.1 per cent of sodium benzoate.

Licensed under U. S. patent 2,480,743.

DIPHTHERIA TOXOID-U.S.P. (See New and Nonofficial Remedies 1949, p. 496).

The following dosage form has been accepted:

CUTTER LABORATORIES, BERKELEY 1, CALIF.

Diphtheria Toxoid: 1.5 cc. vials (one immunization) and 15 cc. vials (ten immunizations). Preserved with thimerosal 1:10,000.

FURTRETHONIUM IODIDE (See THE JOURNAL, Sept. 24, 1949, p. 264).

The following dosage form has been accepted:

SMITH, KLINE & FRENCH LABORATORIES, PHILADELPHIA 1

Ophthalmic Solution Furmethide Iodide 10%: 15 cc. bottles with dropper stopper: A solution containing 0.1 Gm. of furtrethonium iodide in each cc. Preserved with thimerosal 1:100,000.

U. S. patent 2,185,220; U. S. trademark 381,093.

PENICILLIN FOR PARENTERAL USE IN AQUEOUS SOLUTION (See New and Nonofficial Remedies 1949, p. 150).

The following dosage form has been accepted:

SCHENLEY LABORATORIES, INC., NEW YORK 1

Crystalline Potassium Penicillin G: 2,000,000 units in 50 cc. vials.

ALUMINUM HYDROXIDE GEL-N. N. R. (See New and Nonofficial Remedies 1949, page 333).

The following dosage form has been accepted:

THE VALE CHEMICAL CO., INC., ALLENTOWN, PA.

Tablets Aluminum Hydroxide Gel: 0.324 Gm.

THIAMINE HYDROCHLORIDE-U.S.P. (See New and Nonofficial Remedies 1949, page 549).

The following dosage form has been accepted:

VANPELT & BROWN, INC., RICHMOND 4, VA.

Tablets Thiamine Hydrochloride: 5 mg. and 10 mg.

CORRECTION

Through error, in the monograph for Progesterone (THE JOURNAL, March 18, page 817) there appears the following statement:

"The aqueous suspension is four times as active as the oil solution, so that in the latter form, larger doses of the oil solution are required to produce effects equivalent to those obtained with smaller doses of the aqueous suspension. This difference is only quantitative."

This statement as well as the dosage differential between the two forms has not been substantiated and is being withdrawn from N. N. R. 1950.

R. T. STORMONT, M.D., *Secretary.*

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SATURDAY, APRIL 22, 1950

INFANT DEATHS FROM SUFFOCATION

The Statistical Bulletin of the Metropolitan Life Insurance Company for November 1942 issued a warning on the increase of accidental deaths in earliest childhood. The circular predicted that 2,600 children under 1 year of age would be killed accidentally in 1942. The greatest hazard encountered by infants according to this information is that of smothering. The Committee on Public Health Relations of the New York Academy of Medicine [1] stated that deaths from mechanical suffocation have increased by almost 60 per cent in the past decade. They accounted for more than 1,500 deaths in the United States in 1942. Dr. Harold Abramson [2] stated that about 80 per cent of these deaths in New York City for the five year period 1939-1943 occurred in children of less than 1 year of age and 85 per cent of those during the first year of life were in children less than 6 months old. It is significant that the peak of infant deaths from mechanical suffocation was reached during the late fall and early winter months.

A Current Comment in THE JOURNAL, Dec. 8, 1945, called attention to a statement by Davison,[3] coroner of Birmingham, England, to the effect that statistics relating to infant suffocation are misleading, because of overestimation. Thus, during the years 1938 to 1944, 318 infant deaths considered as possibly due to asphyxia were reported to the coroner. Of these infants only 38 were shown to have died of asphyxia. The remaining 280 deaths were of natural causes, principally bronchopneumonia, often associated with otitis media. Davison stresses that a postmortem examination is indispensable as part of the routine examination in every case in which suffocation is considered a likely cause of death. Since this procedure was adopted in Birmingham, in 1929, there has been a decided decrease in infant deaths due to suffocation.

Werne and Garrow,[4] of the Office of Chief Medical Examiner, City of New York, have investigated during the past 15 years 167 consecutive cases of infants under 1 year of age found dead in a crib, carriage or bed while in apparent good health. In not a single instance has their investigation proved accidental mechanical suffocation of a healthy infant by bedclothes or in analogous manner. In 43 of these 167 cases the autopsy alone established the presence of a fatal disease. In the remaining 124 cases with insufficient gross findings to explain death, complete microscopic studies as a rule revealed acute inflammation of the respiratory tract in association with other significant visceral changes. The diagnoses included tonsillitis, laryngotracheitis, bronchitis, bronchiolitis, interstitial pneumonia and hemorrhagic bronchopneumonia not grossly detectable. Lesions were frequently found in the brain, liver, kidneys and lymphatic vessels. These lesions, they stress, were conspicuously absent from the tissues of 31 infants dying of proved violence. These authors also investigated 67 other cases of infants who had been observed to die suddenly and unexpectedly in circumstances in which there could be no possible allegation of smothering. The usual cause of death was acute respiratory disease. The gross anatomic findings of diseases causing death were mastoiditis and otitis media, "idiopathic" cardiac hypertrophy, congenital heart disease, bronchopneumonia, lobar pneumonia, interstitial pneumonitis, bilateral adrenal hemorrhage due to conditions such as meningococcemia and meningitis.

Bowden [5] of Melbourne, Australia, stresses that when a previously apparently healthy infant is found dead face down in bed, or on his back with the bedclothes over his head, it should not be concluded that he has suffocated without a thorough postmortem examination. In many of these sudden deaths no gross abnormalities will be found on ordinary microscopic examination of the organs, and if the pathologist does not pursue his investigation beyond this stage he will diagnose too many accidental suffocations. If he is content only with a thorough postmortem microscopic investigation, including organs which appear to the naked eye to be normal, and if he enlists the aid of other workers, such as the biochemist and bacteriologist, he will rarely diagnose accidental suffocation from bedclothes. From his studies of the sleeping habits of 100 normal babies Bowden concludes that a healthy baby can take care of himself; there is virtually no risk of accidental suffocation from the bedclothes.

At a conference on Sudden Death in Infants held under the auspices of the Children's Bureau and the

1. Infant Deaths from Mechanical Suffocation, Annual Report, New York Academy of Medicine, 1945, p. 40.
2. Abramson, H.: Accidental Mechanical Suffocation in Infants, J. Pediat. **25**: 404 (Nov.) 1944.
3. Davison, W. H.: Accidental Infant Suffocation, Brit. M. J. **2**: 251 (Aug. 25) 1945.
4. Werne, J., and Garrow, I.: Sudden Deaths of Infants Allegedly Due to Mechanical Suffocation, Am. J. Pub. Health **37**: 675 (June) 1947.
5. Bowden, K.: Sudden Death or Alleged Accidental Suffocation in Babies, M. J. Australia **1**: 65 (Jan. 21) 1950.

National Institutes of Health (Nov. 30, 1949), Dr. Katherine Bain [6] summed up the situation as follows: "Each year in the United States a large number of babies under 1 year of age die of what is classified as 'accidental mechanical suffocation.' The story behind the death is usually this: An infant, in apparent good health and usually between the ages of 2 and 5 months, is put to bed in a crib or baby buggy, or in bed with his parents. Several hours later the infant is found dead. Sometimes he is lying on his face; sometimes bedclothes are over his head. Often in the excitement of the discovery the exact conditions are unnoted. The physician, the coroner or the medical examiner, confronted with such a death, is likely to assume that the baby has smothered. And without an autopsy, or at best after a sketchy one, he writes on the birth certificate that the baby's death was due to 'accidental mechanical suffocation.' The mother and father of a baby who has died in this way develop a great sense of guilt, which may disturb their lives for years. But there is now abundant evidence that most of these deaths are not due to any external cause but may be the result of a sudden overwhelming infection with which a young baby is not able to cope. When a careful postmortem examination is made, including a microscopic study, evidence of infection is often found in the baby's respiratory tract, though sometimes elsewhere in his body, as in the membranes of the brain. When a careful history is taken, information is often brought out concerning respiratory infection in the family, and there may be some indication that the baby himself had not been up to par."

Efforts to prevent sudden death of infants should be directed toward diminishing exposure to known sources of infection during this highly vulnerable period of infant life and to the education of parents in the early signs of acute respiratory disease and their significance.

6. Bain, K.: When a Baby Dies Unexpectedly, Child **14**: 130 (March) 1950.

LIVER FUNCTION AND LIVER STRUCTURE

A correlation between morphologic alterations of the liver and the clinical picture and the laboratory findings is difficult, in fact, impossible sometimes. For the pathologist it is in many instances difficult to decide whether the gross and microscopic picture of the liver indicates a fatal hepatic insufficiency. More obscure at present is the correlation between the morphologic changes and the results of the various hepatic tests. Few of these tests measure a basic function of the liver which no other organ performs. Most of them concern determinations of biochemical or serologic changes which occur in various hepatic disorders, but often also in other conditions. The claim has been made repeatedly that no correlation can be made between the histologic picture and the results of the hepatic tests. Nevertheless, it is obvious that some kind of correlation must exist between the deranged hepatic function, apparent from clinical or laboratory findings, and alteration of the histologic picture. The difficulty lies in the recognition of this correlation.

With the recently expanded use of the liver biopsy it has been possible to compare the histologic picture with the results of hepatic tests performed simultaneously with the biopsy. This avoids the confusion that has been produced by the functional and anatomic changes which the liver undergoes in the agonal period as well as by the decomposition of the liver after death. These processes render observations in necropsy material difficult to interpret. One approach to such a correlation is the observation of the coincidence of anatomic, clinical and functional changes in the same patient, based particularly on multiple biopsy studies during the course of the disease.[1] Another approach correlates the statistical coincidence of various morphologic features with the results of tests on a large amount of material, without reference necessarily to the diagnosis. Obviously, much overlapping will occur.

On the basis of such studies [2] a statistically significant correlation was found between diffuse liver cell damage and the albumin-globulin ratio, cephalin flocculation, thymol turbidity and sulfobromophthalein retention. The correlation with other tests was less significant or absent. Focal necrosis or diffuse fatty metamorphosis, even if histologically conspicuous, failed to reveal a correlation. Regeneration coincided best with increased thymol turbidity; cirrhosis formation coincided with elevated cephalin flocculation, thymol turbidity and sedimentation rate, while Kupffer cell activity was related to elevated serum bilirubin and reduced albumin-globulin ratio. Subsequently, the degree of morphologically recognizable liver cell damage was statistically correlated with the degree of abnormality of various tests.[3] This quantitative correlation was significant with an increase in cephalin flocculation, thymol turbidity, total and direct bilirubin and with a decrease in albumin and albumin-globulin ratio. Abnormal results of other tests, such as elevation of serum alkaline phosphatase and urinary urobilinogen, were associated with the presence of liver cell damage but did not measure its degree. However, these general coincidences do not necessarily apply to every disease. For instance, even in severe liver cell damage in the presence of a noninfected extrahepatic biliary obstruction the results of flocculation tests may be normal.

1. Sherlock, S. P. V.: Biochemical Investigations in Liver Disease: Some Correlations with Hepatic Histology, J. Path. & Bact. **58**: 523, 1946. Watson, C. J., and Hoffbauer, F. W.: Liver Function in Hepatitis, Ann. Int. Med. **26**: 813, 1947. Volwiler, W.; Jones, C. M., and Mallory, T. B.: Criteria for the Measurement of Results of Treatment in Fatty Cirrhosis, Gastroenterology **2**: 164, 1948. Kinsell, L. W.; Weiss, H. A.; Michaels, G. D.; Shaver, J. S., and Barton, H. C., Jr.: Correlation of Hepatic Structure and Function, Am. J. Med. **6**: 292, 1949.

2. Franklin, M.; Popper, H.; Steigmann, F., and Kozoll, D. D.: Relation between Structural and Functional Alterations of the Liver, J. Lab. & Clin. Med. **33**: 435, 1948.

3. Popper, H.; Steigman, F., and Szanto, P. B.: Quantitative Correlation of Morphologic Liver Changes and Clinical Tests, Am. J. Clin. Path. **19**: 710, 1949.

A statistical analysis indicates only an association and not a causative relation. Nevertheless, it permits expectation of certain morphologic changes from the results of the hepatic tests. It may aid, therefore, in the practical evaluation of the hepatic tests and in the establishment of the functional significance of histologic features. So far these studies have emphasized the importance of diffuse damage of hepatic epithelial cells for many of the tests. Although the conclusions drawn so far are not final, the correlation between hepatic function and structure appears now less hopeless than it did several years ago. Eventually, such studies may lead to a systematic utilization of the hepatic tests in the clinical management of hepatobiliary diseases.

Current Comment

ACTH IN OPHTHALMOLOGY

Elsewhere in this issue are three papers on the use of pituitary adrenocorticotropic hormone (ACTH) in medicine. Two of these papers report observations made on the treatment of diseases of the eye. The reports are preliminary and are not intended to suggest the routine use of this hormone in ophthalmologic conditions; they are offered to permit the readers of THE JOURNAL to see the extent to which this remarkable hormone is being studied. As one author states, the series is far too small to permit any conclusions. Nevertheless, a new field of exploration is offered for researchers who are experienced and qualified in this field. Time will reveal the full therapeutic possibilities. Until then the use of ACTH in ophthalmologic conditions must be regarded as still in the experimental stage.

USE OF RADIOACTIVE ISOTOPES

A special committee of the American Academy of Pediatrics for the study of radiation effects in childhood has recommended that research study with radioactive isotopes should not be undertaken on pregnant women unless the study cannot be undertaken on animals and unless the study is approved by the Committee for Human Use of Radioactive Isotopes of the Atomic Energy Commission. This recommendation was made because of the current availability of some radioactive isotopes. Such actions seem appropriate at this time. Frank H. Krusen has pointed out,[1] "Until more is known concerning the immediate and remote effects of radioisotopes, it will be well for all institutions which are employing atomic energy, either for treatment or for experimentation, to have a team of workers including, at least, a radiologist, an internist and a physiologist to provide the necessary safety precautions and to control all methods of using atomic energy." The Advisory Committee on the Medical Aspects of Atomic Energy of the Council on Physical Medicine and Rehabilitation has been asked to prepare a report on the dangers of atomic energy as employed in medicine. Until more information on the dangers of atomic energy is available, much caution should be exercised to prevent the indiscriminate use of radioactive substances either in treatment or in research.

1. Krusen, F. H.: Atomic Energy in Medical Practice, M. Clin. North America **31**: 972 (July) 1947.

SAFEGUARDS IN BOXING

The somewhat peculiar hazards of boxing have been called to the attention of the medical profession and the public over a period of years in publications of the American Medical Association.[1] Through its radio programs and transcription series the Association also has warned of the specific dangers.[2] The inherent risk attached to any activity in which the head is often the target for blows has been emphasized, and the need for the most stringent kind of supervision, if the sport is to be conducted at all, has been stressed. The Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association has passed a resolution disapproving boxing as an interschool activity. The Committee based its action primarily on the premise that boxing is one of the few sports in which the offensive goal is to strike the opponent and in which the head is a principal target. There is a resultant potential of permanent injury to the central nervous system, particularly the brain, that may eventuate in a loss of mental power and physical coordination. Realizing that boxing would be continued, the Committee also outlined exacting health and safety precautions that should be taken when the activity is conducted. It was the feeling of the Committee, however, that few schools are in a position to provide the essential equipment and facilities, the trained teaching personnel and the careful medical supervision needed to assure optimum conditions of safety for participants. Professional boxing and amateur boxing conducted outside the school, under a variety of sponsorships, are somewhat different. The contestant is usually more mature and chooses to participate "on his own" and without the stimulus furnished by the sanction and implied approval of an educational institution. Nevertheless, the sport in all its ramifications demands the closest kind of supervision and control. Recent ring deaths, usually following brain injury, have spurred regulatory bodies to careful scrutiny of boxing codes in various states. No amount of regulation can completely remove the hazards of the activity, but every effort must be made to provide the safest possible competitive conditions. The New York State Boxing Commission through its Medical Advisory Board has recently set up a strict code for medical supervision of boxers and wrestlers participating under its jurisdiction. Dr. Frank R. Ferlaino, chairman of the board, in reporting the action expresses the hope that the new regulations will safeguard the health of the athletes concerned and reduce accidents before, during and after bouts. A digest of the code will be found on page 1304.

1. Martland, H. S.: Punch Drunk, J. A. M. A. **91**: 1103 (Oct. 13) 1928. Romino, J. D.: Boxing and Intracranial Injuries, West Virginia M. J. **45**: 19, 1949; abstracted, J. A. M. A. **140**: 652 (June 18), 1949. Gorman, T.: Death in the Ring, Hygeia **27**: 384 (June), 1949.

2. Punch Drunk, Doctors Today series, American Medical Association Broadcasts over National Broadcasting Company network, 1948 (Jan. 31), no. 195. To Box or Not to Box, Your Child Goes to School, radio transcription series, American Medical Association, Bureau of Health Education, 1949, no. 2.

ORGANIZATION SECTION

Official Notes

GROWTH OF HEALTH COUNCILS

Community health councils in the nation have increased from 82 to nearly 300 in the last two years, according to a recent survey by the American Medical Association's Council on Medical Service. Local achievements of the community health councils in the last five years include construction of hospitals with the aid of the Hospital Survey and Construction Act (Hill-Burton Act); increasing available hospital beds; developing clinics; securing more doctors, dentists, nurses and other needed personnel; development of full time local public health services; health examination of children of school and preschool age and correction of their remediable health defects; promotion of voluntary prepayment medical care and hospitalization; provision of medical care for the aged and chronically ill, and meeting costs of medical service to families unable to pay hospital and doctor bills. Councils have matched government funds to pay mental health clinic personnel and conducted educational campaigns to acquaint communities with the value and manner of operation of the clinics. Health councils have been especially important in bringing better medical care to the people of rural communities. The A.M.A.'s efforts to promote organization of community health councils to improve medical care for rural communities date back five years, to the organization of the association's Committee on Rural Health. Since that time it has been actively engaged in coordinating the efforts of farm groups and state and local medical societies in rural health.

Washington Letter

(From a Special Correspondent)

April 17, 1950.

Hearings on Health Bills

The health legislation subcommittee of the Senate Labor and Public Welfare Committee will meet in open session April 24 to hear testimony by Senator Lester C. Hunt (Democrat, Wyoming) in support of his bill which would establish a department of health and initiate a government-sponsored voluntary health insurance program.

On April 25 the subcommittee will launch three days of hearings on a bill for establishment of a United Medical Administration along lines recommended last year by the Hoover Commission. May 9-10 are the dates scheduled for taking of testimony on a bill introduced by Senator Hubert H. Humphrey (Democrat, Minnesota) to authorize federal financial aid to health cooperatives and certain prepayment medical care plans. On May 8 the subcommittee, whose chairman is Senator James E. Murray (Democrat, Montana), will meet in executive session to discuss the Douglas bill on research into child health and welfare.

Controversy Over Hospitals' Closing Still Unsettled

Reconsideration by the Department of Defense management committee of Secretary Louis Johnson's order closing five army and navy hospitals was promised recently to the chairman of a special congressional committee investigating the closings. It was deemed unlikely, however, that Defense would accede to the committee's request that all five institutions be kept in commission.

Conflicting opinions as to the savings which would be effected by the hospital cutback, including reduction in status of thirteen facilities besides the five to be closed outright, were presented to the House subcommittee on armed services appropriations. Although the hearing was held March 30 in executive session, the transcript was not made public until April 8. Witnesses included Rear Admiral Clifford A. Swanson, Navy Surgeon General; Dr. Richard L. Meiling, medical director in the Department of Defense, and Dr. H. A. Press, director of management and planning in Veterans Administration.

Secretary Johnson had stated the hospital retrenchment would save $25,000,000 annually, but Assistant Secretary W. J. McNeil testified that the saving would be slightly over $6,000,000 in the first year. Admiral Swanson, referring to McNeil's estimate that $715,000 of this amount would accrue to navy department economy, asserted flatly that it would be more than offset by terminal leave payments, added transportation costs and numerous other extra expenses.

The Surgeon General, noting that the House Appropriations Committee reduced the navy's budget by $4,000,000 on the supposition that millions would be saved by the hospital retrenchment program, warned that, unless full restoration is made, provision of essential medical services will have to be curtailed.

Dr. Press testified that deactivation of the five hospitals and reduction of thirteen others in size would result in allocation of beds for Veterans Administration patients being reduced to 3,585. At present 6,335 beds in army and navy hospitals are allocated for veterans.

General Romulo Carries Terramycin to Philippines

Gen. Carlos P. Romulo, ambassador from the Philippines and president of the United Nations General Assembly, left Washington by plane for his homeland on April 11, carrying with him 5,000 capsules of terramycin (antibiotic produced by Streptomyces rimosus) for emergency treatment of typhus, undulant fever and other diseases. It was a gift from the drug's manufacturer, Charles Pfizer & Co., of Brooklyn.

"This shipment of terramycin which I am taking with me," said General Romulo, "is symbolic of what the United Nations Organization means in its basic human, not political, endeavors. During the Japanese occupation we lost a number of our finest medical institutions and hundreds of our ablest clinicians. This, plus the fact that we are a poor country, explains why we do not have, either in kind or in number, sufficient hospitals, doctors and trained technicians. Neither do we have the newest drugs, such as terramycin. As a consequence, thousands of lives are needlessly lost each year."

Medical Defenses Against A-Bomb Warfare

The Joint Congressional Committee on Atomic Energy has made public the testimony—edited so as to exclude security-classified information—presented to its members in executive session on March 30 by Dr. Norvin C. Kiefer, director, Health Resources Division, National Security Resources Board. His testimony dealt with mobilization and coordination of all resources for saving of life and treatment of casualities in event of an atomic bomb attack.

Special problems now under study, said Dr. Kiefer, include collection of blood and blood derivatives, standardization of treatment of burns, evacuation of casualties, prevention of spread of diseases from animals to man and strengthening of industrial hygiene. Steps are being taken, he added, to declassify certain data on biologic warfare to permit distribution among state and local public health authorities. He also noted that courses of instruction have been started to teach physicians, dentists, nurses and allied personnel the fundamentals of radiologic defense.

Antihistamine Hearings Scheduled

The Federal Trade Commission has announced it will hold hearings April 28 on its separate complaints against Bristol-Myers Co. and Anahist Co., Inc., for their advertising claims in connection with marketing of Resistab and Anahist, respectively. Both companies are charged with misrepresenting therapeutic properties of the antihistamine products, the complaints being the first of their kind to be issued.

As a result of the Commission's investigation, the following conclusions were drawn and are set forth in the complaint against Bristol-Myers:

Resistab is neither a cure nor an adequate treatment for the common cold or its symptoms, it is not a preventive against infection or its manifestations, it will not arrest a cold's development even if dosage is taken early and it may be unsafe and harmful even when the drug is taken as directed.

Regarding Anahist, advertising claims that it was tested by the Navy Medical Corps are challenged by the Federal Trade Commission and branded as false. The complaint also denies that such initial manifestations of a cold as sneezing, coughing and nasal discharge are due to presence in nose and throat of excessive amounts of histamine, as claimed in the firm's advertisements.

"The use of Anahist in no way contributes to the operation of the defense mechanism of the body against its invasion by the cold virus," says the complaint. "The body has no 'natural defense' against the manifestations of the common cold except its ability to overcome the causative infection and this will be in no way assisted by the use of Anahist."

The Federal Trade Commission has scheduled May 19 for a hearing on its complaint against Union Pharmaceutical Co., centering around charges that advertising claims for the antihistamine product "Inhiston" are false and misleading.

Another antihistamine product was cited March 24 when the Federal Trade Commission issued a complaint against Whitehall Pharmacal Co. for its advertising campaign in behalf of Kriptin. The government charges are similar to those filed against Resistab and Anahist. The sole active ingredient of the Whitehall firm's tablets is 25 mg. of pyranisamine maleate, according to the complaint.

Another April complaint by the Federal Trade Commission was directed at a Chicago group, trading as Dr. Ritholz & Sons Co., whose marketing of devices for self testing of visual acuity was described as deceptive.

The commission approved a stipulation in which J. C. Eno, Inc., of Bloomfield, N. J., agree to modify claims for "Eno's Effervescent Salt."

Coming Medical Meetings

Aero Medical Association, Chicago, May 29-31. Dr. Thomas H. Sutherland, 214 S. State St., Marion, Ohio, Secretary.

American Association of Industrial Physicians and Surgeons, Chicago, Hotel Sherman, April 24-28. Dr. Frederick W. Slobe, 28 E. Jackson Blvd., Chicago 4, Secretary.

American Association of Genito-Urinary Surgeons, Hershey, Penn., Hotel Hershey, May 24-26. Dr. Norris J. Heckel, 122 S. Michigan Ave., Chicago 3, Secretary.

American Association of the History of Medicine, Boston, May 21-23. Dr. Benjamin Spector, 416 Huntington Ave., Boston 15, Secretary.

American Association on Mental Deficiency, Columbus, Ohio, Hotel Deshler-Wallick, May 16-20. Dr. Neil A. Dayton, P. O. Box 96, Willimantic, Conn., Secretary.

American Broncho-Esophagological Association, San Francisco, Mark Hopkins Hotel, May 25-26. Dr. Edwin N. Broyles, 1100 N. Charles St., Baltimore 1, Secretary.

American Congress on Obstetrics and Gynecology, New York, Hotel Pennsylvania, May 14-19. Dr. F. Bayard Carter, Duke Medical School, Durham, N. C., Secretary.

American Gastro-Enterological Association, Atlantic City, April 28-29. Dr. Dwight L. Wilbur, 655 Sutter St., San Francisco, Secretary.

American Gastroscopic Society, Atlantic City, April 28-29. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.

American Geriatrics Society, New York, Hotel Commodore, June 1-3. Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

American Gynecological Society, White Sulphur Springs, W. Va., The Greenbrier, May 11-13. Dr. Norman F. Miller, 1313 E. Ann St., Ann Arbor, Mich., Secretary.

American Hearing Society, Chicago, Drake Hotel, June 15-17. Mrs. Frances E. Lee, 817 Fourteenth St., N.W., Washington 5, D. C.

American Laryngological Association, San Francisco, May 23-24. Dr. Louis H. Clerf, 128 S. Tenth St., Philadelphia 7, Secretary.

American Laryngological, Rhinological and Otological Society, San Francisco, May 25-27. Dr. C. Stewart Nash, 277 Alexander St., Rochester 7, N. Y., Secretary.

American Neurological Association, Atlantic City, Claridge Hotel, June 12-14. Dr. H. Houston Merritt, 710 W. 168th St., New York 32, Secretary.

American Ophthalmological Society, Hot Springs, Va., The Homestead, May 31-June 2. Dr. Maynard C. Wheeler, 30 W. 59th St., New York 19, Secretary.

American Orthopedic Association, Virginia Beach, Va., May 23-26. Dr. C. Leslie Mitchell, Henry Ford Hospital, Detroit 2, Secretary.

American Otological Society, San Francisco, May 21-22. Dr. Gordon D. Hoople, 1100 E. Genesee St., Syracuse 10, N. Y., Secretary.

American Pediatric Society, French Lick, Ind., May 8-10. Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12, Secretary.

American Psychiatric Association, Detroit, May 1-5. Dr. Leo H. Bartemeier, General Motors Bldg., Detroit 2, Secretary.

American Psychoanalytic Association, Detroit, Hotel Statler, April 28-30. Dr. LeRoy M. A. Maeder, 1910 Rittenhouse Square, Philadelphia 3, Secretary.

American Psychosomatic Society, Atlantic City, Chalfonte-Haddon Hall, April 29. Dr. Sydney G. Margolin, 714 Madison Ave., New York 21, Secretary.

American Radium Society, New York, Roosevelt Hotel, May 25-26. Dr. Hugh F. Hare, 605 Commonwealth Ave., Boston 15, Secretary.

American Society for Clinical Investigation, Atlantic City, May 1. Dr. Paul B. Beeson, Grady Hospital, Atlanta 3, Ga., Secretary.

American Urological Association, Washington, D. C., Hotel Statler, May 29-June 1. Dr. Charles H. deT. Shivers, Boardwalk National Arcade Bldg., Atlantic City, N. J., Secretary.

Arizona State Medical Association, Phoenix, Hotel Westward Ho, April 30-May 4. Dr. Frank J. Milloy, 234 N. Central Ave., Phoenix, Secretary.

Association for Physical and Mental Rehabilitation, Memphis, Tenn., Hotel Peabody, May 23-27. Mr. Benjamin Forman, 57 Granger St., Canandaigua, N. Y., Secretary.

Association of American Physicians, Atlantic City, May 2-3. Dr. Henry M. Thomas Jr., 1201 N. Calvert St., Baltimore 2, Secretary.

California Medical Association, San Diego, April 30-May 3. Dr. L. Henry Garland, 450 Sutter St., San Francisco, Secretary.

Connecticut State Medical Society, Waterbury, May 2-4. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Secretary.

Florida Medical Association, Hollywood, April 23-26. Dr. Robert B. McIver, P. O. Box 1018, Jacksonville, Secretary.

Hawaii Territorial Medical Association, Hilo, May 4-7. Dr. I. L. Tilden, Mabel Smyth Bldg., Honolulu 13, Secretary.

Illinois State Medical Society, Springfield, Illinois State Armory, May 23-25. Dr. Harold M. Camp, 224 S. Main St., Monmouth, Secretary.

International and Fourth American Congress on Obstetrics and Gynecology, New York, Hotel Pennsylvania, May 14-19. Dr. Fred L. Adair, 161 E. Erie St., Chicago 11, Information Headquarters.

International Congress on Asthma, Mont Dore, France, June 3-4. Secretariat, 59 rue Bonaparte, Paris, France.

Iowa State Medical Society, Burlington, April 23-26. Dr. Allan B. Phillips, 406 Sixth Ave., Des Moines 9, Secretary.

Kansas Medical Society, Wichita, May 15-18. Dr. D. D. Vermillion, 512 New England Bldg., Topeka, Secretary.

Louisiana State Medical Society, Baton Rouge, April 24-26. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans 13, Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Baltimore, April 25-26. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

Massachusetts Medical Society, Boston, Hotel Statler, May 16-19. Dr. H. Quimby Gallupe, 8 Fenway, Boston 15, Secretary.

Minnesota State Medical Association, Duluth, June 12-14. Dr. B. B. Souster, 496 Lowry Medical Arts Bldg., St. Paul 2, Secretary.

Mississippi State Medical Association, Jackson, May 9-11. Dr. T. M. Dye, Box 295, Clarksdale, Secretary.

National Tuberculosis Association, Washington, D. C., April 25-28. Dr. James E. Perkins, 1790 Broadway, New York 19, Managing Director.

Nebraska State Medical Association, Lincoln, Hotel Cornhusker, May 1-4. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln, Secretary.

New Jersey, Medical Society of, Atlantic City, Haddon Hall, May 22-24. Dr. Marcus H. Greifinger, 315 W. State St., Trenton 8, Secretary.

New Mexico Medical Society, Las Cruces, May 4-7. Dr. H. L. January, 4852 Southern Ave., Albuquerque, Secretary.

New York, Medical Society of the State of, New York, May 8-12. Dr. Walter P. Anderton, 292 Madison Ave., New York 17, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, The Carolina, May 1-3. Dr. Millard D. Hill, 15 W. Hargett St., Raleigh, Secretary.

North Central Clinical Society, Cincinnati, Netherland Plaza Hotel, April 29. Dr. John H. Payne, 5 W. Fourth St., Cincinnati, Secretary.

North Dakota State Medical Association, Grand Forks, May 27-30. Dr. O. A. Sedlak, 702 First Ave. S., Fargo, Secretary.

Ohio State Medical Association, Cleveland, May 16-19. Mr. Charles S. Nelson, 79 E. State St., Columbus 15, Executive Secretary.

Oklahoma State Medical Association, Oklahoma City, May 14-17. Dr. Lewis J. Moorman, 210 Plaza Court, Oklahoma City, Secretary.

Rhode Island Medical Society, Providence, R. I. Medical Library, May 10-11. Dr. Morgan Cutts, 106 E. Francis St., Providence 3, Secretary.

Society of American Bacteriologists, Baltimore, May 15-19. Dr. John E. Blair, 1919 Madison Ave., New York 35, Secretary.

South Carolina Medical Association, Myrtle Beach, May 16-18. Dr. Julian P. Price, 105 W. Cheves St., Florence, Secretary.

South Dakota State Medical Association, Mitchell, May 20-23. Dr. Roland G. Mayer, 22½ S. Main St., Aberdeen, Secretary.

Texas, State Medical Association of, Fort Worth, May 2-5. Dr. Harold M. Williams, 700 Guadalupe St., Austin, Secretary.

Western Branch, American Public Health Association, Portland, Ore., May 30-June 1. Mr. Walter S. Mangold, University of California, Berkeley, Calif., Secretary.

GOVERNMENT SERVICES

ARMY

SUMMER TRAINING FOR RESERVISTS

The Fifth Army's medical reservists will spend two weeks in practical field training this summer at Camp McCoy, Wis. Trainees will study camouflage, field fortifications, arctic and tropical warfare and defense against chemical, mechanized, aircraft and atomic attacks. The 14 day training cycle will be given twice—July 16 to 29 and July 30 to August 13—and is to be staged and directed by members of the 301st Hospital Center, a Chicago reserve medical unit, under the leadership of Brig. Gen. Carl L. Steinhoff of 6207 North Artesian Avenue, Chicago. Specialists from the Surgeon General's office in Washington will discuss topics of current interest to the medical corpsmen. Among those who will attend the Camp McCoy sessions is Col. W. L. Wilson, special assistant to the Surgeon General for Civil Defense, Washington, D. C. Two hundred and sixty-four officers, enlisted men and Army nurses from 13 medical units in Fifth Army's area are scheduled to attend the two week sessions.

TEMPORARY PROMOTIONS

Nominated by the President for temporary promotion in the Medical Department were Brigadier Generals Leonard D. Heaton and Arthur R. Gaines, both to the rank of major general, and Colonels James P. Cooney and Maxwell G. Keeler, to the rank of brigadier general. The nominations are awaiting confirmation by the Senate. General Heaton, since 1946, has been chief of the surgical service at Letterman General Hospital, San Francisco. He has been in the regular Army since 1927. General Gaines is now commanding Brooke General Hospital, Fort Sam Houston, Texas. He entered the Army in 1917 and was certified by the American Board of Internal Medicine in 1944. Colonel Cooney is now chief of the Radiological Branch, Division of Military Application, U. S. Atomic Energy Commission. Colonel Cooney entered the service in 1927. He is a specialist certified by the American Board of Radiology. Colonel Keeler is at present commanding Madigan General Hospital, Tacoma, Wash. He was commissioned in the regular Army in 1920. Shortly after the Pearl Harbor attack, he assumed command of the 5th General Hospital in Europe, remaining there until October 1944, when he became commanding officer of the 803rd Hospital Center in the same theater.

GENERAL ROBERTS RETIRES

A review at Fitzsimons General Hospital honored Brig. Gen. Edwin H. Roberts, hospital commander, on his retirement on March 31 after 32 years' service with the Medical Department. Among the distinguished guests present for the ceremony was Governor W. Lee Knous of Colorado. During World War II, General Roberts commanded the 208th and 95th General Hospitals. He returned to the States in March 1945 and directed the inactivation of Thayer General Hospital and, later, Lovell General Hospital and then was appointed deputy commissioner and chief of professional services at Percy Jones General Hospital, Battle Creek, Mich. He is a specialist certified by the American Board of Internal Medicine. Col. Howard W. Doan, who has served as deputy commander under General Roberts, has been appointed as temporary commanding officer.

CERTIFICATIONS BY SPECIALTY BOARDS

Five medical officers have recently been certified by American specialty boards:

Col. William A. Todd Jr., surgery; Col. Vernon J. Erkenbeck, otolaryngology; Lieut. Col. Rickard P. Mason, preventive medicine and public health; Lieut. Col. Charles W. Hoffman Jr., urology, and Major Robert D. Anderson, orthopedic surgery.

PERSONAL

Col. James P. Cooney (MC), chief, Radiology Branch, Division of Military Application, Atomic Energy Commission, discussed "Problems of the Physician in Atomic Warfare" before the Canadian Association of Radiologists, in Montreal, January 5.

NAVY

CORRESPONDENCE COURSES

Two additional correspondence courses are available for distribution to qualified naval reserve and regular medical department personnel.

Title of Course	Promotion Units	Retirement Points	Eligible Personnel
Radiological Defense and Atomic Medicine	3	36	MC, DC, MSC, NC, HC (officers only)
Insect, Pest and Rodent Control	2½	32	MC, DC, MSC, NC, HC (officers and enlisted)

Application for enrolment should be made to the Bureau of Medicine and Surgery via appropriate official channels.

WOMAN DOCTOR ORDERED TO SEA DUTY

According to the Bureau of Medicine and Surgery, Lieut. Comdr. Bernice R. Walters (MCR), who is under orders to report to the U. S. Navy Hospital Ship *Consolation* late this summer, is the first woman doctor ever ordered to duty aboard a Navy ship. Dr. Walters received a B.S. degree in 1932 from Long Island University and an M.D. from Woman's Medical College of Pennsylvania. She completed an internship in 1937 at St. Francis Hospital, La Crosse, Wis. After two years' residency training, she was in private practice until her appointment in the Naval Reserve in 1943. She served during World War II and volunteered for return to active duty in 1948. Dr. Walters holds a private pilot's license.

PERSONAL

Comdr. John W. Metcalfe (MC, USN) has been nominated for duty under instruction in a residency in orthopedic surgery, Naval Hospital, San Diego, Calif., where he is now stationed.

Lieut. (jg) Thomas C. Beaman, of Memphis, Tenn., and Lieut. (jg) Lewis C. Lohoff, of Hutchinson, Kan., have been nominated for active duty as interns in naval hospitals.

Comdr. George M. Bell and Lieut. Comdr. Max O. Sartori have been nominated for duty under instruction in the Navy's Graduate Training Program to a residency in orthopedic surgery and to a residency in surgery, respectively, at Naval Hospital, Oakland, Calif.

Capt. F. R. Lang, Comdr. Joseph J. Timmes and Comdr. Howell E. Wiggins have been certified by the American Board of Preventive Medicine and Public Health in the Founders Group, American Board of Surgery and the American Board of Orthopedic Surgery, respectively.

Comdr. Howard A. Johnson and Lieut. Comdr. Ralph D. Ross have been nominated for duty under instruction in the Navy's Graduate Training Program to a residency in surgery, Naval Hospital, Portsmouth, Va., and to a residency in internal medicine, Naval Hospital, San Diego, Calif., respectively.

The following medical officers have been certified by the specialty boards indicated: Capt. Frank P. Kreuz Jr. and Comdr. John S. Thiemeyer Jr., American Board of Orthopedic Surgery, and Lieut. John B. Reddy, American Board of Otolaryngology.

PUBLIC HEALTH SERVICE

APPOINT CONSULTANTS ON NUTRITION

The appointment of eight physicians as consultants on nutrition to the Public Health Service, in order to broaden the effectiveness of technical assistance to states and local communities, was announced March 30. The newly appointed consultants are: Dr. Frederick J. Stare, professor of nutrition, Harvard University, Boston; Dr. Norman Jolliffe, director, Bureau of Nutrition, New York; Dr. A. Hughes Bryan, professor of nutrition, School of Public Health, University of North Carolina, Chapel Hill, N. C.: Dr. Richard W. Vilter, associate professor of medicine, University of Cincinnati, Cincinnati; Dr. Robert E. Shank, professor of preventive medicine, Washington University, St. Louis; Dr. William J. Darby, director, Division of Nutrition, Vanderbilt University, Nashville, Tenn.; Dr. Philip C. Jeans, head of department of pediatrics, State University of Iowa, Iowa City, and Dr. Grace A. Goldsmith, professor of medicine, Tulane University, New Orleans.

DR. M. I. SMITH RETIRES

Dr. Maurice I. Smith, chief pharmacologist in the Public Health Service has retired after 30 years of research with the National Institutes of Health and its predecessor, the Hygienic Laboratory. While Professor of Pharmacology at the University of Nebraska Medical School, Dr. Smith accepted a temporary position with the Public Health Service in 1918, two years later he accepted a permanent position at the Hygienic Laboratory. He was born in Russia and received his M.D. degree from Cornell University Medical School. The next three years he was an instructor at the University of Michigan Medical School; from there he went to the University of Nebraska. Dr. Smith is the author or co-author of 124 scientific papers. He is a member of the American Society for Pharmacology and Experimental Therapeutics, the Society for Experimental Biology and Medicine, the Washington (D. C.) Academy of Science and the American Trudeau Society.

GRANTS FOR WATER POLLUTION STUDIES

Grants totaling $995,427 for water pollution studies have been awarded state and interstate agencies during the first year in which funds have been available. Last of the grants to be approved for the year was $17,774 to Virginia for a study of the effects of industrial waste.

Following are the approved grants:

Arkansas, $17,396: studies of pollution resulting from wastes produced by oil and paper industries, mining operations, canneries and dairy products plants.

California, $27,370: additional personnel and equipment to strengthen existing antipollution programs with particular reference to industrial wastes.

Minnesota, $8,500: studies of treatment of beet sugar refinery wastes.

Ohio, $12,900: studies of the toxicity of electroplating wastes.

Washington, $10,000: studies of the effect of industrial wastes, including paper and pulp mills, on aquatic life.

Atlantic Marine Fisheries Commission, $10,000: compilation of previous pollution surveys of the Atlantic Seaboard, a review of remedies previously proposed or adopted and a study of current production and the economic effects of pollution in fisheries areas as they relate to industrial wastes.

RESEARCH ON KIDNEY CONDITIONS

Three physicians have been appointed to the Research Branch of the National Heart Institute. All will be on the staff of the Section on Kidney and Electrolyte Metabolism. This is the second of five laboratory-clinical sections to be established in the research program of the institute. The three scientists are:

Dr. Ernest Cotlove, a research fellow of the Division of Medical Sciences, National Research Council.

Dr. James O. Davis, formerly on the staff of the Public Health Service Marine Hospital in Baltimore.

Dr. Thomas J. Kennedy Jr., a research fellow with Research Service, First (Columbia) Medical Division, Goldwater Memorial Hospital.

PERSONAL

Dr. Cornelius B. Philip has been named assistant director of the Rocky Mountain Laboratory of the National Institutes of Health, Helena, Mont. He has served as medical entomologist at the Rocky Mountain Laboratory since 1930.

VETERANS ADMINISTRATION

SEMINARS AT VETERANS HOSPITAL, DOWNEY, ILL.

The Veterans Administration Hospital at Downey, Ill., invites physicians and allied personnel to attend the following series of seminars in neuropsychiatry and related fields.

April 12, 1950—Dr. Franz Alexander, director, Chicago Psychoanalytic Institute, and professor of psychiatry, University of Illinois.

April 19, 1950—Dr. J. L. Moreno, director, Psychodramatic Institute, Beacon, N. Y.

April 26, 1950—Dr. Sandor Rado, director of the Post-Graduate Training Neuropsychiatric Institute, Columbia University

May 10, 1950—Dr. Franz Kallmann, director, Department of Medical Genetics, Neuropsychiatric Institute, Columbia University

May 17, 1950—Dr. Ralph W. Gerard, professor of physiology, University of Chicago

May 24, 1950—Dr. Theresa Benedek, training analyst, Chicago Psychoanalytic Institute

May 31, 1950—Dr. Warren S. McCulloch, research professor of neurophysiology, Department of Psychiatry, University of Illinois

June 7, 1950—Dr. Gregory Zilboorg, instructor, New York Psychoanalytic Institute, New York

June 14, 1950—Dr. William Malamud, professor of psychiatry, Boston University School of Medicine

June 21, 1950—Dr. Frieda Fromm Reichmann, training analyst, Washington-Baltimore Psychoanalytic Institute

Date to be announced—Dr. Karl Menninger

Each speaker will conduct a seminar or demonstration at the hospital at 10 a. m. and 2 p. m. and at 8 p. m. will deliver a lecture at the Veterans Administration Regional Office, 366 West Adams Street, Chicago 6. There will be no charge for this series. Further information may be obtained by writing to Byron S. Cane, M.D., Manager.

BIDS FOR HOSPITAL CONSTRUCTION

The Veterans Administration is accepting sealed bids for a new 1,000 bed hospital in Salisbury, N. C., that will involve nearly 10,000,000 cubic feet of construction and will be erected on a 41 acre site in the northwestern section of the city, consisting of 17 buildings and eight connecting tunnels. The project includes an administration building, medical and surgical building, two admissions buildings, cafeteria and kitchen, recreation and occupational therapy and apartment buildings. The buildings are to have concrete foundations, brick-faced exterior walls with stone trim and backed with hollow tile, reinforced concrete floors and built-up roofs. Because the Salisbury hospital is to be built in as short a period as possible, bids will be evaluated on the basis of time as well as amount of money. Bids, prepared in triplicate, should be submitted to the Director, Construction Service, Veterans Administration, Washington 25, D. C., by 1:30 p. m., April 25, 1950.

PERSONAL

Dr. Michael L. Matte will succeed Dr. Robert C. Cook as manager of the Veterans Administration hospital at Fort Logan, Colo., effective January 22. Dr. Cook will become assistant chief medical director in the central office of the Veterans Administration. Dr. Matte has been chief medical officer at the Veterans Administration Center, Wood, Wis.

Dr. Delmar Goode has been named manager of the Little Rock Hospital, Arkansas. He formerly was medical director, supervising activities of hospitals in and around Washington, D. C.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ARIZONA

State Medical Meeting.—The Arizona Medical Association will hold its annual meeting at the Westward Ho Hotel in Phoenix April 30-May 3, under the presidency of Dr. Robert S. Flinn, Phoenix. Guest speakers at the general sessions include:

John M. Waugh, Rochester, Minn., Indications for Operation and the Management of Peptic Ulcer.
George C. Griffith, Pasadena, Calif., Treatment of Edema.
Harry B. Macey, Temple, Texas, Low Back Pain.
Stephen R. Elek, Los Angeles, Functional Heart Disease.

The dinner dance will be held Tuesday evening. Several state specialty societies and the Western Orthopedic Association will meet in conjunction with the state association. The Woman's Auxiliary will meet May 1-3 at the hotel.

ARKANSAS

Grant for Pediatric Pavilion.—A gift of $500,000 from the William Buchanan Foundation of Dallas, Texas, will provide a pediatric floor in the new medical center in Little Rock, to be known as the William Buchanan Pavilion for Children. This grant with matching federal funds will allow construction increasing the bed capacity of the new hospital from 400 to 500. In addition, a rapid treatment unit for neuropsychiatric patients will be provided. Plans for the new hospital and University of Arkansas School of Medicine building are being drawn, and construction will begin before the end of 1950.

COLORADO

Outbreak of Animal Rabies.—An outbreak of animal rabies in the four county area comprising metropolitan Denver has been reported. The four county statistics for recent years show no cases in 1944 and 1945, 5 in 1946, 11 in 1947 and 2 in 1948. From October 1949 through March 18, 1950, 70 cases have been reported, 55 cases having occurred since January 1, all in domestic dogs, with the exception of 2 in cats. Twenty-four persons in Denver proper and 33 in the immediately adjoining counties have been reported to the Colorado Health Department as undergoing treatment after bites by rabid dogs. Ernest S. Tierkel, D.V.M., who is Rabies Control Consultant of the U. S. Public Health Service's Communicable Disease Center at Atlanta, Ga., is temporarily in Denver advising state and local health officials and professional organizations regarding the epidemic.

CONNECTICUT

New Hartford Hospital.—Constructed at a cost of $1,700,000, the 115 bed Mount Sinai Hospital of Hartford opened March 19. Officials hope within a few years to add a fifth floor to the rear building to serve 150 patients. Complete medical and surgical service will be provided in emergency and outpatient departments. The maternity department, which has not been part of the hospital since 1943 because of lack of room, provides for 21 mothers and 27 infants.

IDAHO

Hospital News.—Dr. Wallace Bond, Twin Falls, councilor for the Southern District, represented officers and the Idaho State Medical Association at the dedication of the new Bear Lake Memorial Hospital, Montpelier, March 19. The new $360,000 hospital has a bed capacity of 35.

Tuberculosis Mobile Unit.—The Idaho State Anti-Tuberculosis Association has purchased a mobile unit to be staffed and operated cooperatively with the Idaho Department of Public Health. The unit is scheduled to be delivered July 1. An advisory committee from the Idaho Medical Association will be appointed to assist in formation of policy and over-all development of the program.

Personal.—Dr. Frederick O. Graeber of Vale, Ore., has been appointed director of maternal and child health, Idaho Department of Public Health, to succeed Dr. Madelene M. Donnelly, Boise, who has resigned. Dr. Graeber has been director of the Malheur County Health Department for the past 15 months. He is a graduate of the University of Minnesota Medical School (1939) and received his master's degree in public health from Johns Hopkins University, Baltimore.——Dr. Robert S. McKean of Boise is the new Idaho chairman of the Mid-Century White House Conference on Children and Youth, appointed by Governor C. A. Robins. Dr. McKean is a member of the American Academy of Pediatrics, served in the navy during the war and is active in the Idaho State Medical Association.

ILLINOIS

Hospital News.—Carthage Memorial Hospital, construction of which was begun in July 1949, will be ready to admit patients early this fall. It is a beautifully designed, one story structure, with facilities for 50 patients, being built at a cost of $732,568.

Chicago

Dr. Coulter's Books Presented to Northwestern.—One of the country's finest collections of books on physical medicine, owned by Dr. John S. Coulter, who died in December 1949, has been presented to the Northwestern University Medical School. In 1926 Dr. Coulter was appointed assistant professor of physical medicine at Northwestern and became a full professor and chairman of the department in 1943. The gift will be placed in the Archibald Church Library.

Professor Heads Army Hospital Reserve Unit.—Lieut. Col. Robert B. Lewy, clinical assistant professor of otolaryngology at the University of Illinois College of Medicine and a member of the faculty since 1937, has been appointed commanding officer of the 427th General Hospital, a 1,000 bed U. S. Army reserve unit sponsored by the university. Colonel Lewy formerly served in the dual capacity of executive officer and chief of ophthalmology and otolaryngology for the hospital; he succeeds Col. John B. Youmans. The 427th General Hospital, which was activated at the university in 1948, is staffed by 52 medical, dental and administrative officers and nurses.

Northwestern University Alumni Reunion.—The annual Medical Faculty Alumni Reunion of Northwestern University Medical School will be held June 3 at the Furniture Club, 888 Lake Shore Drive, with a social period beginning at 5:30 p. m. followed by dinner at 7 o'clock. Dr. Thomas C. Douglass, vice president in charge of activities, is chairman of the function. Representatives of the classes of 1905, 1910, 1915, 1920, 1925, 1930, 1935, 1940 and 1945 will have special tables at the dinner, and members of the classes of 1895 and 1900 and this year's graduating class will be honored guests. Reservations may be made through the office of the association, Room 796, Montgomery Ward Building, 303 E. Chicago Ave. Reservations for dinner are $6 each.

IOWA

County Society News.—At the meeting of the Dubuque County Medical Society April 11 Dr. Arthur H. Conley, associate professor orthopedics and attending surgeon at the Cook County Hospital in Chicago, spoke on "Fractures."

Hospital News.—The construction of the million dollar, 133 bed Ottumwa general hospital began March 19, to replace the present obsolete 57 bed building constructed in 1904. Hundreds of persons of the community have contributed funds to make the nonprofit hospital possible.

KENTUCKY

Dr. Thomas Walker State Park.—The bicentennial of the entrance into Kentucky of Dr. Thomas Walker and five companions is being observed the last three days of April in a celebration centering around Dr. Thomas Walker State Park, near Barbourville. Nineteen years ahead of Daniel Boone, Dr. Walker and his companions crossed through Cumberland Gap into an unbroken forest wilderness as the first white men to set foot in Kentucky. On the north bank of the Cumberland River, which they named, they erected a cabin, a replica of which now stands on the site of the 12 acre state park donated in 1931 by the Barbourville Post of the American Legion.

LOUISIANA

State Medical Meeting in Baton Rouge.—The Louisiana State Medical Society will hold its annual meeting at the Heidelberg Hotel in Baton Rouge April 24-26, under the presidency of Dr. Edwin H. Lawson, New Orleans. Out of state speakers will be:

Grant H. Laing, Chicago, Systemic Nutritional Disturbances Reflected in the Mouth.
J. Garrott Allen, Chicago, Surgical Lesions of the Colon and Rectum.
Saul Hertz, Boston, Role of Radioactive Isotopes in Clinical Medicine.
Claude G. Callender, Jackson, Miss., The Diagnosis of Ectopic Pregnancy.
Edward H. Ray, Lexington, Ky., Recent Experiences with Transurethral Prostatectomy.
William A. Reilly, Little Rock, Ark., Pediatric Endocrine Problems.

The President's Ball will be held at La Tropicana on Tuesday at 9 p. m. Exhibits will be shown. The Woman's Auxiliary will meet in conjunction with the state association.

MINNESOTA

Mental Health Bulletin.—*Mental Health Progress*, a four page bulletin of the Minnesota Department of Health and the state university, appeared March 1, to be published monthly except during July and August. It will present a summary of the developments in the field of mental health. Special emphasis will be placed on preventive and educational work.

Low Maternal Mortality Rate.—Maternity Hospital in Minneapolis has reported that it has established what is believed to be a record, 6,845 consecutive maternity cases without a maternal death. The record ran between April 1930 and August 1947. During the past 13 years there were only 3 maternal deaths in 13,009 cases, a rate of 0.023 per 1,000. The national average in maternal mortality is 1.3 deaths per 1,000.

Personals.—Dr. Charles W. Mayo, professor of surgery at the Mayo Foundation and surgeon at the Mayo Clinic, Rochester, visited Tripler General Hospital in Honolulu recently. Dr. Mayo was a colonel in the U. S. Army Medical Corp during the late war and has a distinguished record of service in the South Pacific area.——Edward C. Kendall, Sc.D., and Dr. Philip S. Hench, both of Rochester, received bronze replicas of a printer's composing stick on April 14 at the Hotel Astor in New York City, awarded by the New York City chapter of the American Newspaper Guild, for their work in the discovery and clinical application of cortisone. The award is one of eleven conferred on persons in special fields for their "contributions to social or cultural progress."——Dr. Thomas B. Magath, Rochester, has resigned from the State Board of Health, of which he has been president since 1940. He has been associated with the Mayo Clinic since 1919 and is now head of the division of clinical laboratories.

MISSOURI

Establish Thompson Lecture.—Dr. Frederick G. Thompson of St. Joseph is being honored by a lectureship established in consideration of his 60 years of practice. Dr. John M. Waugh, Rochester, Minn., will speak May 4 on "Indications for Surgical Treatment of Peptic Ulcer."

General Practice Meeting.—The Missouri Academy of General Practice will hold its annual meeting in Springfield April 27 at the Kentwood Arms Hotel. Dr. R. B. Robbins, Camden, Ark., speaker of the House of Delegates of the national academy, will be the principal speaker at a 6 p. m. dinner. A scientific session will be presented beginning at 2:30 p. m.

First Spector Lecture.—The Saint Louis University School of Medicine initiated the Hyman Spector Lecture Series April 12, when Dr. J. Arthur Meyers of Minneapolis, spoke on "Immunity and Tuberculosis—Thirty years of Observation." The series was named for the late Dr. Hyman Spector, formerly assistant professor of internal medicine at the university.

Dr. Royston Feted.—One hundred and fifty members of the medical profession attended a dinner March 1 at the Missouri Athletic Club in St. Louis honoring Dr. Grandison D. Royston, who is retiring after 43 years as obstetrician, gynecologist and teacher. Dr. Royston, a member of the Washington University School of Medicine faculty for 38 years, is moving to his farm near Texarkana, Ark.

NEW YORK

Mental Health Commissioner Resigns.—Dr. Frederick MacCurdy, state commissioner of mental health since June 1943, resigned April 1 to accept an appointment from Governor Dewey as medical consultant to the New York State Citizens' Committee of One Hundred for Children and Youth. The committee will work with the National White House committee in developing research and fact finding that the state will submit as its contribution to the Mid-Century White House Conference on Children and Youth, which will open December 3 in Washington, D. C.

New Cancer Study Center.—Financed by a $435,000 grant from the U. S. Public Health Service, a new center for cancer research, control and teaching was opened April 5 at the University of Rochester School of Medicine and Dentistry. The University of Rochester Medical Center has carried on an extensive program of cancer investigation for 25 years. The new cancer unit will bring closer teamwork of allied research and services, including diagnostic, consultative and therapy services, and the work with clinical radioactive isotopes for cancer therapy which will be centered in the new medical atomic energy building now nearing completion. The ground floor of the new cancer center is devoted to tumor clinics and allied facilities. The second floor includes a metabolism ward and laboratories. One of the new research devices in the new building is a $15,000 ultracentrifuge for studies of the proteins in the human body. On the third floor are laboratories of the Division of Cancer Research. Other facilities include conference rooms, offices of epidemiology and statistics, private examining rooms, conference rooms and an office for social workers. An important feature of the new cancer unit is its arrangements for keeping thorough records on every case.

Conference on Mental Hygiene.—The fourth annual Conference on Mental Hygiene and Problems of Exceptional Children will be held at Syracuse University in Syracuse May 12-13. The program will be devoted to the prevention of maladjustment. The lecturers include: Stanley G. Estes, Ph.D., Harvard University, Boston; Dr. Bela Mittelmann, New York University; David Rapaport, Ph.D., Austin Riggs Foundation, Stockbridge, Mass., and Fritz Redl, Ph.D., Wayne University, Detroit. Saturday lecturers will be Wendell Johnson, Ph.D., of the University of Iowa, Iowa City; Dr. Lauretta Bender, New York University, New York; Kimball Young, Ph.D., Northwestern University, Evanston, Ill., and Ralph Linton, Ph.D., of Yale University, New Haven, Conn.

New York State Medical Meeting.—The annual meeting of the Medical Society of the State of New York will be held May 8-12 at the Hotel Statler in New York, under the presidency of Dr. John J. Masterson, New York. Those speaking by invitation at the general sessions Wednesday and Friday afternoons include:

Alfred Gilman, Ph.D., New York, Pharmacologic Agents Which Modify Autonomic Function.

Laurence H. Snyder, Sc.D., Norman, Okla., The A. Walter Suiter Lecture, Practical Application of Recent Advances in Genetics to Clinical Problems.

Television demonstrations of operations and clinical treatments will be presented from 12 noon to 2 p. m. on Wednesday through Friday in the Keystone Room under the supervision of the Long Island College of Medicine and sponsored by E. R. Squibb & Sons, in cooperation with the Radio Corporation of America. A Teaching Day for postgraduate medical education will be held May 9. In the morning rehabilitation of the chronically disabled will be discussed by Drs. Alfred L. Lane, Rochester; Arthur S. Abramson, Bronx, and George G. Deaver, Donald A. Covalt and Mr. Earle Daniel of New York. The afternoon panel discussion will be on chronic alcoholism as a medical problem, the participants being Drs. C. Nelson Davis, Merion, Pa.; Harry M. Tiebout, Greenwich, Conn.; Marvin A. Block, Buffalo; James J. Smith, New York; I. Jay Brightman, Albany, and a co-founder of Alcoholics Anonymous. Section meetings will be held Wednesday morning, all day and evening Thursday, and Friday morning. Scientific and technical exhibits will be shown. The annual banquet will take place in the Penn Top Wednesday at 7 p. m. The Woman's Auxiliary will meet May 7-8.

New Medical Regulations for Boxing and Wrestling.—The Medical Advisory Board of the New York State Athletic Commission has announced a new set of medical rules and regulations for boxers and wrestlers who participate under its jurisdiction. A comprehensive initial medical examination is to be required prior to licensing boxers and wrestlers. An examination will also be mandatory with the renewal of the license each year. In addition, all contestants will be given an examination at the noon weighing-in on the day of the contest and another just prior to the bout. For championship or important matches a further special examination five days before the contest will be required. Injuries or illness suffered while in training for a match must be reported and followed up with appropriate medical appraisal and recommendations. When any question arises as to the physical ability of a contestant to participate safely, a panel of physicians designated by the Medical Advisory Board will make the final decision after reexamination of the athlete. During bouts the ringside attending physician may enter the ring between rounds to evaluate the apparent or latent injury. When in his judgment the contestant is in danger of serious injury, he shall advise the referee that the contest be terminated. After a knockout or in the case of severe injury the ringside physician will render emergency care and make recommendations for further treatment or hospitalization. The physician may require that the participant remain in the arena after the contest long enough for necessary emergency care, observation and advice. Any contestant having a severe injury not requiring hospitalization must be reexamined within a 24 hour period. Also contained in the regulations are special stipulations to be invoked after a series of losses or after severe injury or knockout to prevent cumulative injury. Methods of reporting the results of examinations, the record of injuries and their treatment and, in fact, the complete participation record of the athlete are designed to provide the commission with the essential tools for determining within human limitations the fitness of contestants to

take part in boxing and wrestling contests with the greatest possible degree of safety. The nine man Medical Advisory Board to the state boxing commission was created by state law in 1948 (THE JOURNAL, Nov. 13, 1948, page 831). Dr. Frank R. Ferlaino, New York, is board chairman.

New York City

Chest Conference.—The Sixth Annual Chest Conference at St. John's Hospital in Brooklyn will be held May 18 at 8:30 p. m. Dr. C. Rollin Hanlon will speak on "Surgery of Congenital and Acquired Heart Disease."

Lectures on Oral Surgery.—Dr. Theodor Blum and Lester R. Cahn, D.D.S., will lecture on "A Plea for Conservatism in Oral Surgery" at the next monthly conference of the New York Institute of Clinical Oral Pathology, April 24 at the New York Academy of Medicine, Room 440 at 9 p. m.

Course in Surgical Anatomy.—This course will be given at Cornell University Medical College from June 1 through June 30. Designed for candidates for the American Board of Surgery, it will consist of an intensive review of surgical anatomy with demonstrations and dissection. Dr. Ernest W. Lampe will be in charge. Tuition is $200, and registration is limited to 25. Inquiries may be directed to Office of the Dean, Cornell University Medical College, 1300 York Avenue, New York 21.

Lecture Series on Viruses.—Dr. Salvador E. Luria, associate professor of bacteriology at Indiana University, Bloomington, was chosen to deliver the 1950 Jesup Lectures, in Schermerhorn Hall at Columbia University beginning April 10 and extending through April 24. Sponsored by the department of zoology at Columbia, the Jesup Lectures were established in 1905 in honor of Morris Ketchum Jesup, New York banker who died in 1908. Dr. Luria, a member of the Indiana faculty since 1943, received his medical degree at the University of Turin, Italy, and came to the United States in 1940. Previously he studied in Rome under Enrico Fermi, Nobel prize winner in physics, and at the Institute of Pasteur in Paris. He is a specialist in the study of viruses.

NORTH CAROLINA

Society News.—At the annual meeting of the South Atlantic Association of Obstetricians and Gynecologists in Roanoke, Va., February 9-11 the following officers were elected: Drs. Lester A. Wilson, Charleston, S. C., president; Emmett D. Colvin, Atlanta, Ga., president-elect, and John C. Burwell Jr., Greensboro, N. C., secretary-treasurer. The 1951 annual meeting will be held February 8-10 at the Ormond Beach Hotel and Country Club, Ormond Beach, Fla.

Cancer Detection Mobile.—A new gastric cancer detection mobile, equipped with a Schmidt-Helm camera for photofluorography, began its tour of the state's 10 clinics March 7. The mobile will stay about three months at each clinic. Two radiology consultants of Watts Hospital and Duke University, Durham, will render diagnosis and refer those requiring treatment to their physicians. Two years ago the state inaugurated an accelerated screening program that provides examinations of the five most common cancer sites for women over 35 and men over 40.

State Medical Meeting at Pinehurst.—The Medical Society of the State of North Carolina will hold its annual session at the Hotel Carolina in Pinehurst May 1-3, under the presidency of Dr. G. Westbrooke Murphy, Asheville. Guest speakers include:

George F. Lull, Secretary and General Manager, American Medical Association, Chicago.
Elmer Hess, Erie, Pa., Corporate Practice of Medicine in the Relationship of Hospitals and the Profession.
J. Warrwick Thomas, Richmond, Va., Gastrointestinal and Food Allergy; Diagnosis and Treatment.
Eugene P. Pendergrass, Philadelphia, Role of the Physician in the Diagnosis of Breast Carcinoma.

Section meetings will be held. At the president's dinner Tuesday at 7 p. m. Mr. John McPherrin, editor, *American Druggist*, New York, will speak on "The British Health Scheme."

OKLAHOMA

Lecture on Rheumatism.—Dr. W. Paul Holbrook, Tucson, Ariz., will address the Oklahoma Rheumatism Society on "The Use of ACTH and Cortisone (Compound E)" at the Biltmore Hotel, Oklahoma City, June 4. This is the day preceding the annual state meeting. Dr. Holbrook is now president of the National Arthritis and Rheumatism Foundation and is a former president of the American Rheumatism Association.

Lectures in Tulsa.—Dr. Frederick A. Coller, chairman, department of surgery, University of Michigan Medical School, Ann Arbor, will be the guest speaker for the Tulsa County Medical Society April 24 at the Mayo at 8 p. m. He will speak on "Use and Abuse of Parenteral Fluids." The Oklahoma Medical Research Foundation is sponsoring a lecture April 25 at the university auditorium at 4 p. m. when Dr. Harold L. Sheehan, professor of pathology at the University of Liverpool, England, will speak on the "Physiopathology of the Pituitary and Clinical Aspects of Hypopituitarism."

TEXAS

Course in Management of Pain.—Southwestern Medical School of the University of Texas, Dallas, will present a course in the management of pain at the Veterans Administration Hospital in McKinney May 5-7. The course is limited to 30 physicians, and the registration fee is $5. Registrations close April 15.

University Lectures.—Col. Elbert DeCoursey of the Army Medical Center, Washington, D. C., spoke at the University of Texas Medical Branch, Galveston, on April 3 on "Medical Aspects of Atomic Radiation." Dr. Sam L. Clark, professor of anatomy at Vanderbilt University School of Medicine, Nashville, Tenn., and president of the American Anatomical Association, spoke recently to the staff and students on "Life Within the Brain." The annual Sigma Chi Lecture at the University of Texas Medical Branch was presented April 3 by Olaf Larsell, Ph.D., professor of anatomy at the University of Oregon Medical School, Portland. Dr. Larsell described the nerve supply to the lung and its biologic significance.

WEST VIRGINIA

Organize Diabetes Group.—A state diabetes association will be organized during the annual meeting of the West Virginia State Medical Association at White Sulphur Springs in July, when a constitution and by-laws will be presented for adoption. All doctors desiring to become members are requested to write to the Diabetes Committee, care of the West Virginia State Medical Association, Box 1031, Charleston.

Public Health Appointments.—Dr. Benjamin M. Drake, director of Rockingham-Caswell Health Department, Wentworth, N. C., has been appointed deputy health officer. Dr. Henry C. Huntley of Adrian, Mich., has been appointed director of disease control. Both positions are included in the reorganization program of the state department of health approved at the 1949 sessions of the legislature. Dr. Drake has been in public health work since 1937. Dr. Huntley began his public health work in 1942 as a health officer of Oklahoma and for the past three years has been serving as a health officer in Michigan.

GENERAL

New Translation Service.—A service of translation, English-French, specializing in medical articles, has recently been created by Domus Medica, at 111 East Oak Street, Chicago. It offers to physicians and medical societies carefully worked out translations supervised by physicians.

Meeting on Mental Deficiency.—The American Association on Mental Deficiency will meet at the Deshler-Wallick Hotel in Columbus, Ohio, May 16-20. In addition to the general sessions, section meetings will be held each day. Round-table breakfasts and luncheons have been scheduled.

Society News.—The southern Tri-State Medical Association at its meeting in Fayetteville in February installed Dr. Richard B. Davis of Greensboro, N. C., as president, chose Dr. William R. Wallace of Chester, S. C., as president-elect and re-elected Dr. James M. Northington of Charlotte, N. C., secretary-treasurer for his twenty-sixth term. The next annual meeting will be held in Columbia, S. C.

College Health Association.—The twelfth annual meeting of the North-Central section of the American College Health Association is being held at the University of Wisconsin, April 21-22 with Dr John W. Brown, chairman of the university department of preventive medicine and director of student health and president of the association, presiding. Delegates are from Iowa, Minnesota, North Dakota, South Dakota and Wisconsin.

International Congress of Internal Medicine.—This congress is to be held in Paris September 11-14. Speakers from the United States registered for the program are Drs. Selman A. Waksman, New Brunswick, N. J.; Byron E. Hall, Rochester, Minn.; George W. Thorn, Boston; Milton B. Plotz, Brooklyn, and William J. Kerr, San Francisco. General secretary of the International Congress of Internal Medicine is Dr. L. Justin-Besancon, 38 Rue Barbet de Jouy, Paris 7, France.

Dr. Alvarez to Edit *GP*.—Dr. Walter C. Alvarez, Rochester, Minn., has been appointed medical editor of *GP*, published by the American Academy of General Practice. Dr. Alvarez was selected to succeed Dr. F. Kenneth Albrecht, who died recently after an automobile accident. He has been associated with the Mayo Clinic since 1926. Having reached retirement age at the Mayo Foundation, Dr. Alvarez is moving to Chicago, where he will assume the duties of medical editor of *GP*.

Appoint Chief of Liaison Office of WHO.—Dr. P. M. Kaul of India has been appointed chief of the New York Liaison Office of the World Health Organization. In 1947, when he was deputy director general of health, he was loaned by the Indian Government to WHO to become director of the Singapore Epidemiologic Intelligence Station. He has served as secretary of the WHO Expert Committee on Plague, the Joint Study Group on Cholera of WHO and the International Office of Public Hygiene. Dr. Kaul obtained his M.D. degree from the Medical School of the University of Punjab, did postgraduate studies at Guy's Medical School and Hospital, London, and received his training in public health at the London School of Hygiene. He is a member of the British Royal College of Physicians, London.

American Gynecological Society.—The annual meeting of this society will be held May 11-13 at the Greenbrier, White Sulphur Springs, W. Va., under the presidency of Dr. Joseph L. Baer, Chicago. The preliminary program lists the following invited speakers:

Woodward D. Beacham, New Orleans, La., Sickle Cell Disease and Pregnancy.
David N. Danforth, Evanston, Ill., Cervical Changes During Pregnancy.
Russell R. de Alvarez, Seattle, Renal Function in Pregnancy Toxemias.
J. Robert Wilson, Philadelphia, Hysterectomy.
Allan C. Barnes, Columbus, Ohio, Use of Radioactive Cobalt in Treatment of Carcinoma of Cervix.
Frank R. Lock, Winston-Salem, N. C., Method of Diagnosis of Functional Pelvic Disease.

The guest speaker will be Dr. Austin M. Brues, Chicago, director of the biology division, Argonne National Laboratory, Chicago, who will talk on "The Place of Radioactive Isotopes in Therapy."

American Psychoanalytic Association.—The annual meeting of this association will be held at the Hotel Statler in Detroit, April 27-30, under the presidency of Dr. M. Ralph Kaufman, New York. Invited speakers include:

Anna Freud, London, England, Problems of Child Analysis.
Richard E. Renneker, Chicago, Pre-Sleep Mechanisms of Dream Control.
Thomas S. Szasz, Chicago, Oral Mechanisms in Constipation and Diarrhea.

Subjects of panel discussions on Saturday are: The interaction of social and deep psychologic factors, provocation and manifestations of anxiety in schizophrenia, problems of character analysis, psychoanalysis and developmental psychology.

American Gastroenterological Association.—This association will hold its annual meeting at the Hotel Claridge in Atlantic City, N. J., April 28-29, under the presidency of Dr. J. Arnold Bargen, Rochester, Minn. Papers being presented on invitation by a single author include:

Mr. Dane G. Prugh, Boston, Influence of Emotional Factors on the Course of Ulcerative Colitis in Children.
Wyman P. Sloan, Rochester, Minn., Life Histories of Patients with Ulcerative Colitis.
E. Leonard Posey Jr., Jackson, Miss., Metabolic Derangements in Chronic Ulcerative Colitis.
Karl Meyer, New York, Lysozyme and Ulcerative Alimentary Disease.
Miss Frances H. Smith, Boston, Potassium Metabolism in Gastrointestinal Problems.
O. Roger Hollan, Philadelphia (Research Fellowship), Site of Formation of Urobilinogen in the Intact Human Gastrointestinal Tract.
Eddy D. Palmer, Washington, D. C., Error in Gastroscopic Diagnosis: Consideration of Sources.
John W. Findley Jr., Phoenix, Ariz., Atrophic Gastritis: Follow-Up Study of 100 Patients.

The annual dinner will be held Saturday at 8 p. m., when the Julius Friedenwald Medal will be presented to Dr. B. B. Vincent Lyon, Philadelphia. The dinner address will be given by Harold E. Stassen, president of the University of Pennsylvania, Philadelphia, on "Freedom and Medicine."

Science Awards of the Institute of Nutrition.—Three science awards were announced by the American Institute of Nutrition. Conrad A. Elvehjem, Sc.D., chairman of the department of biochemistry at the University of Wisconsin, was selected to receive the Osborne and Mendal Award "in recognition of his contributions to our knowledge of the vitamin and amino acid requirements of experimental animals." The award, made possible by the Nutrition Foundation, is in recognition of recent basic research regarded by the institute as having greatest significance in any area of the science of nutrition. Recipient of the Mead Johnson Vitamin B-Complex Award for 1950 is Dr. William B. Castle of Harvard Medical School, Boston, "in recognition of his classic investigations leading to the concept of intrinsic and extrinsic factors in pernicious anemia, and of his studies elucidating the relation of vitamin B_{12} to this concept." The 1950 Borden Award in Nutrition was presented to Henry C. Sherman, D.Sc., professor emeritus of Columbia University "for research emphasizing the nutritive importance of components of dairy products." The awards were presented at the annual meeting of the institute in Atlantic City April 19.

Congress of International Congress of Psychiatry.—This congress is to be held at the Sorbonne, Paris, France, September 18-27. The scientific afternoon sessions have been divided into the following sections for discussion:

Psychopathology of Delusions, Ferdinand Morel, Geneva, chairman; speakers: P. Guiraud, Paris; W. Mayer-Gross, Dumfries, Scotland; E. Morselli, Novara, Italy; H. C. Rumke, Utrecht, Holland.
The Application of Mental Tests to Clinical Psychiatry, Honorio Delgado, Lima, chairman; speakers: M. Bleuler, Zurich, Alfredo Guera, Madrid; R. Myssen, Brussels; P. Pichot, Paris; David Rapaport, Ph.D., Stockbridge, Mass.
Cerebral Anatomy and Physiology in the Light of Lobotomies and Topectomies, Frederick L. Golla, London, chairman; speakers: H. J. deBarahona Fernandes, Lisbon; Walter Freeman, Washington, D. C.; Alfred Meyer, London.
Indications of Shock Therapy Methods, Josef Handelsman, Varsovia, chairman; speakers: U. Cerletti, Rome; Rysrard Dreszer, Poznam; M. Fiamberti, Vareze, Italy; Juan Lopez Ibor, Madrid; L. Meduna, Chicago; Manfred Sakel, New York.
Evolution and Present Trends of Psychoanalysis, Franz Alexander, Chicago, chairman; speakers: Anna Freud, London; Maurice Levine, Cincinnati; Raymond de Saussure, New York.
Genetics and Eugenics, Torsten Sjogren, Stockholm, chairman; speakers: Franz Kallmann, New York; Lionel Penrose, London; J. A. Fraser-Roberts, London; Elio Slater, London; Erik Stromgren, Risskov.

Morning sessions will consider further the discussions of previous afternoons. A series of debates will also be held. The registration fee is 6,000 francs for members and 3,000 francs for associate members. The general secretary is Dr. Henri Ey, and the congress address is Congres International de Psychiatrie, 1, rue Dabanis, Paris 14.

FOREIGN

Smallpox in Scotland.—A Reuters dispatch from Glasgow, Scotland, dated April 2, reported that 22 cases of smallpox had developed in the city in four days. The disease was reported brought to the city by an Indian seaman who has recovered. Vaccine was flown from London and other Scottish towns, and thousands of persons waited outside clinics and hospitals for vaccination. All municipal employes in Glasgow have been immunized, and 200 hospitals have been quarantined.

Italian Medical Film Library.—The Mario Donati Foundation for medical and surgical research has instituted a film section in connection with the Educational and Scientific Film Institute. Its aims will be to countenance the diffusion and knowledge of medical and scientific cinema. To this purpose it intends to: (1) make a catalog of all the Italian medical films, covering the existing as well as the current production, (2) organize a medical film library to be kept at disposition of Italian and foreign scientific centers, (3) get in touch with similar foreign institutions and (4) foster and organize national and international shows of medical films. The section will have its office at the Mario Donai Foundation, Milan, Via S. Andrea 6.

CORRECTION

Number of Internships Offered.—In the Annual Report on Internships and Residencies, in THE JOURNAL, April 15, page 1145, the sentence "None the less, virtually the same number of hospitals this year offer 1,372 more internships. . . ." should read: "None the less, virtually the same number of hospitals this year offer 814 more internships. . . ."

Under the list of approved residencies in internal medicine (page 1167), the Veterans Administration Hospital, Fort Howard, Md., which has been temporarily approved by the Council and the American Board of Internal Medicine, was deleted in error.

Marriages

ARTHUR G. SCHWARTZ, Rome, N. Y., to Miss Miriam Lerman of Oneida, January 7.

LEONARD E. FIELD to Miss Beatrice Epstein, both of New York, March 21.

LINUS W. CAVE to Miss Estelle Ann Puisis, both of New Haven, Conn., February 18.

JOHN GORDON HAMILTON to Miss Harriet Ann Davis, both of Rochester, N. Y., February 25.

JOHN POWELL ANDERSON, Louisville, Ky., to Miss Ruth Ann Van Cleve of Berea, December 19.

Deaths

Harry Hamilton Lane ✠ Medical Director, Captain, U. S. Navy, retired, Newport, R. I.; born Jan. 18, 1880; Jefferson Medical College of Philadelphia, 1904; entered the U. S. Navy in 1908 while working in Panama at the Colon Hospital at Cristobal; during World War I served with the Marines in France and also served at Navy headquarters in Paris; was on a tour of duty in Haiti from 1922 to 1925 as assistant sanitary engineer for Haiti; his decorations include the Mexican Campaign Medal, Dominican Campaign Medal, World War I Victory Medal with overseas clasp and two battle clasps and the Abdon Caldron Medal, 2nd class (Ecuador); during his naval career received temporary leave on two occasions to accompany scientific expeditions to islands in the South Pacific; during that time studied tropical diseases and collected specimens for museums and scientific study; in December 1933 was placed on the retired list for physical disability; died in Naval Hospital, Bethesda, Md., March 10, aged 70, of arteriosclerosis and bronchopneumonia.

Frederick Kenneth Albrecht ✠ Baltimore; born in Erie, Pa., April 1, 1910; St. Louis University School of Medicine, 1939; member of the Medical and Chirurgical Faculty of Maryland and the American Trudeau Society; entered the U. S. Public Health Service, serving in various localities during World War II; in 1946 went to Germany as a medical consultant to the state department; resigned from the Public Health Service in 1947 and became an editor for Williams & Wilkins Company, editing their "Current Medical Digest"; in 1949 became director of the division of tuberculosis control, Kansas State Board of Health at Topeka; editor of *GP*; author of "Modern Management in Clinical Medicine"; died in the University Hospital, Ann Arbor, Mich., March 8, aged 39, of pulmonary embolism with infarction as the result of an automobile accident.

Harold Medoris Doolittle ✠ Dallas, Texas; born in Elyria, Ohio, Aug. 27, 1877; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; emeritus professor of surgery at the Southwestern Medical College; on the faculty of Baylor University College of Medicine from 1906 until the school was moved to Houston in 1943; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; past president of the Texas Surgical Society, of which he had been one of the organizers; affiliated with the Dallas Medical and Surgical Clinic Hospital, where he died February 22, aged 72, of diabetes mellitus, hypertension and chronic nephritis.

Wenzel Matthias Wochos ✠ Kewaunee, Wis.; born in Kewaunee, Wis., Aug. 16, 1873; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; member of the American Association of Industrial Physicians and Surgeons; for many years member of the park board and president of the high school board; served as a member of the draft board during World War I and as examining physician for Selective Service during World War II; formerly county physician; for many years director of the Union State Bank; died in St. Vincent Hospital, Green Bay, March 15, aged 76, of coronary occlusion.

Wallace Perry Martin ✠ Clovis, N. M.; born in Evansville, Ind., Oct. 29, 1886; College of Physicians and Surgeons, Los Angeles, 1915; past president of the New Mexico State Medical Society and the Curry County Medical Society; secretary-treasurer of the Curry-Roosevelt County Medical Society; local physician and surgeon for the Santa Fe Railroad; served during World War I; colonel in the New Mexico National Guard and its state medical examiner; an assistant to the state health officer; died in San Antonio, Texas, March 16, aged 63, of coronary occlusion, while attending a conference.

William Alexander Arnold, Camp Hill, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1901; died February 7, aged 80, of arteriosclerotic heart disease.

Carrie B. Banning, Fort Wayne, Ind.; Cleveland University of Medicine and Surgery, 1894; died in February, aged 93, of cancer.

August Frederick Bechtold, Belleville, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1899; member of the American Medical Association; past president of St. Clair County Medical Society; served during World War I; for many years local examiner for the Metropolitan Life Insurance Company; examiner for the John Hancock Insurance Company for the Belleville and East St. Louis areas; died February 28, aged 72, of coronary occlusion.

Fowler Border, Oklahoma City, Okla.; St. Louis College of Physicians and Surgeons, 1900; for many years mayor of Mangum; died January 26, aged 73.

George Russell Campbell, Augusta, Maine; Medical School of Maine, Portland, 1895; member of the American Medical Association; for many years affiliated with Augusta General Hospital, of which he had been one of the organizers and founders; died February 27, aged 82, of carcinoma.

Justin Loomis Christian ✠ Paxtang, Pa.; College of Physicians and Surgeons, Baltimore, 1890; member of the Paxtang Fire Department and Board of Health; died in Harrisburg (Pa.) Hospital February 27, aged 83, of carcinoma of the right parotid gland.

Chelsea Austin Coleman, Dayton, Ohio; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; member of the American Urological Association; fellow of the American College of Surgeons; honorary consultant in urology to the Miami Valley and Good Samaritan hospitals; died in Hollywood, Fla., February 13, aged 65, of coronary thrombosis.

Thomas Benjamin Curran, Victoria, B. C., Canada; Rush Medical College, Chicago, 1899; honorary member of the Washington State Medical Association; member of the American Medical Association; killed February 27, aged 75, when he fell from the tenth story window of a hotel in Seattle.

Earl Emanuel Dale ✠ Dwight, Ill.; Chicago College of Medicine and Surgery, 1917; entered the service of the Army Medical Corps in 1918-1919 as first lieutenant; later rose through the various ranks to that of lieutenant colonel in the medical reserve corps of the Army; served in the outpatient department at the Veterans Administration Hospital in Hines, and as commanding officer of the battalion at Dwight of the Veterans Hospital unit in the Fifth Corps area; died March 6, aged 58, of coronary thrombosis.

Arthur Charles Darrow ✠ San Fernando, Calif.; Washington University School of Medicine, St. Louis, 1936; served during World War II; died February 17, aged 39, of virus pneumonia.

Alletta Bedford Deming, Waterbury, Conn.; Cornell University Medical College, New York, 1905; served on the school board for six years; died January 29, aged 69, of cancer.

Charles W. Dickey, Nashville, Tenn.; University of Nashville Medical Department, 1887; Vanderbilt University School of Medicine, Nashville, 1887; died February 28, aged 88.

Edmund W. P. Downing, Franktown, Va.; College of Physicians and Surgeons, Baltimore, 1886; member of the American Medical Association; died February 28, aged 89, of heart disease.

Arthur Glen Emerson, Bald Knob, Ark.; Omaha Medical College, 1901; died February 2, aged 76, of cerebral hemorrhage.

Paul William Foster, Lewisburg, Tenn.; Vanderbilt University School of Medicine, Nashville, 1924; served during World War I; died February 19, aged 55, of coronary thrombosis.

Robert Brodie Gantt, Charleston, S. C.; Medical College of the State of South Carolina, Charleston, 1914; served as assistant professor of urology at his alma mater; member of the American Medical Association; for many years affiliated with Roper Hospital; died in St. Francis Xavier Infirmary February 24, aged 59, of coronary thrombosis.

Edwin Lincoln Goss, Carrington, N. D.; College of Physicians and Surgeons of Chicago, 1892; served during World War I; past president of the North Dakota State Medical Association; died February 4, aged 84, of coronary thrombosis.

James D. Grant, Longview, Texas; Meharry Medical College, Nashville, Tenn., 1915; died January 27, aged 61.

P. William Haake ✠ Homer, N. Y.; Syracuse University College of Medicine, 1927; on the staff of Cortland County Hospital in Cortland; died January 11, aged 49, of myocardial infarction.

Harper Taliaferro Hamner, Camp Hill, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1889; member of the American Medical Association; died February 10, aged 83, of coronary thrombosis.

Roger Holcomb ✠ Portland, Ore.; Rush Medical College, Chicago, 1924; member of the North Pacific Society of Internal Medicine; served during World Wars I and II; clinical associate at the University of Oregon Medical School; on the staffs of Emanuel Hospital and the Good Samaritan Hospital, where he died February 14, aged 53, of coronary occlusion.

✠ Indicates Fellow of the American Medical Association.

John Holst ✦ Omaha; John A. Creighton Medical College, Omaha, 1913; served during World War I; vice consul for Denmark from 1935 until his resignation on account of ill health in 1949; was knighted by King Frederick of Denmark for his services; in 1948 was made an honorary member of the Norwegian Ophthalmological Society of Oslo; died January 11, aged 64, of heart disease.

William Henry Howard, Oelwein, Iowa; the Hahnemann Medical College and Hospital, Chicago, 1915; member of the American Academy of Ophthalmology and Otolaryngology; died in Knoxville February 11, aged 56, of coronary occlusion.

Clarence David Jacobs, Kingstree, S. C.; University of Nashville (Tenn.) Medical Department, 1905; member of the American Medical Association; served during World War I; died February 26, aged 73, of pulmonary interstitial fibrosis.

James Arthur Jennings ✦ St. Petersburg, Fla.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1898; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; formerly practiced in Chicago, where he taught at the University of Illinois College of Medicine and Rush Medical College; member of the staff of Cook County Hospital from 1905 to 1911 and St. Anthony's Hospital from 1900 to 1930; died April 13, 1949, aged 83, of carcinomatosis.

Paul Hermann Krebs ✦ Cleveland; University of Wooster Medical Department, Cleveland, 1894; served on the staff of the Lutheran Hospital, where he died February 27, aged 79, of arteriosclerotic heart disease.

William W. Lasley, Lewisburg, Ky.; University of Louisville (Ky.) Medical Department, 1885; died in Greenville February 14, aged 97, of uremia.

Wililam Edward Lawhead ✦ P.A.S., Lieutenant, U. S. Navy, retired, Van Wert, Ohio; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; entered the Navy in 1917 and retired March 7, 1925; past president of the Van Wert County Medical Society; served as city and county health officer; affiliated with Van Wert County Hospital; died recently, aged 63, of gastric ulcer.

Donald William Leonard ✦ Exeter, N. H.; Harvard Medical School, Boston, 1929; certified by the National Board of Medical Examiners; deputy medical examiner for Rockingham County; fellow of the American College of Surgeons; on the staff of the Exeter Hospital, where he died February 21, aged 46, of cerebral hemorrhage.

Walter John Le Rossignol ✦ Pomona, Calif.; Gross Medical College, Denver, 1896; member of the Colorado State Medical Society; died February 9, aged 79.

Raymond Francis McAloon, Massena, N. Y.; Albany (N. Y.) Medical College, 1913; member of the American Medical Association; served overseas during World War I; affiliated with Massena Memorial Hospital; died March 5, aged 61, of cerebral hemorrhage.

Frank George McCarthy ✦ Terre Haute, Ind.; Indiana University School of Medicine, Indianapolis, 1909; member of the American Urological Association; died suddenly January 21, aged 68, of coronary thrombosis and hypertension.

Clara Bywater McCraken, Belvidere, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1908; died February 22, aged 84.

William Gansevoort Mack, Skaneateles, N. Y.; Albany (N. Y.) Medical College, 1900; died in the Highland Hospital, Rochester, February 22, aged 84, of acute myocardial infarction.

William Henry Mars, Philadelphia, Miss.; University of Nashville (Tenn.) Medical Department and Vanderbilt University School of Medicine, Nashville, 1892; one of the founders and directors of the Citizens Bank of Philadelphia; died February 21, aged 82, of carcinoma.

George Herbert Miller, Los Angeles; McGill University Faculty of Medicine, Montreal, Que., Canada, 1901; member of the American Medical Association; died in the Good Samaritan Hospital December 20, aged 71.

Raffaele Muojo, Sea Cliff, N. Y.; Regia Universita di Napoli Facolta di Medicina e Chirurgia, Italy, 1896; died December 20, aged 80, of myocardial infarction and coronary sclerosis.

Charles Luman Nichols ✦ Philmont, N. Y.; Albany (N. Y.) Medical College, 1915; on the staff of Hudson City Hospital, Hudson; district school physician; died February 20, aged 56, of myocardial infarction.

Eugene Pile, Ashton, Kan.; Missouri Medical College, St. Louis, 1883; member of the American Medical Association; died in Holton February 14, aged 89, of uremia.

Eugene Olin Porter, Cincinnati; Miami Medical College, Cincinnati, 1908; member of the American Medical Association; surgeon for the Baltimore and Ohio Railroad for many years; died February 6, aged 75, of myocardial infarction.

Harvey Ollis Randel ✦ Oklahoma City, Okla.; Chicago College of Medicine and Surgery, 1915; assistant professor of ophthalmology at the University of Oklahoma School of Medicine; member of the American Academy of Ophthalmology and Otolaryngology; past president of the Oklahoma Society of Ophthalmology; specialist certified by the American Board of Ophthalmology; served during World War I; on the staff of St. Anthony Hospital; died February 17, aged 55, of heart disease.

Clifton Reedy, Columbus, Ohio; Starling Medical College, Columbus, 1897; died January 29, aged 80, of coronary thrombosis.

James Francis Roohan, Saratoga Springs, N. Y.; Long Island College Hospital, Brooklyn, 1912; at one time an officer in the regular army; died December 7, aged 61.

Annie Stevens Rundell, Vassar, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; died February 22, aged 82, of hypostatic pneumonia.

Jacob Sachs ✦ Brooklyn; Cornell University Medical College, New York, 1910; specialist certified by the American Board of Internal Medicine; served overseas during World War I; affiliated with Maimonides Hospital, Israel Zion Division; died in the Fort Hamilton Veterans Administration Hospital February 23, aged 61, of coronary disease.

Leonard Joseph Sagal, New York; Harvard Medical School, Boston, 1945; certified by the National Board of Medical Examiners; served during World War II; formerly an intern at Mount Sinai Hospital, where he was a resident physician and where he died December 8, aged 26, of cerebral vascular accident.

Dick Harold Saley, Northville, Mich.; State University of Iowa College of Medicine, Iowa City, 1919; member of the American Trudeau Society; assistant medical superintendent of the William H. Maybury Sanatorium; died February 28, aged 58, of heart disease and pulmonary emphysema.

Orlando Frank Scott, Bellwood, Ill.; Rush Medical College, Chicago, 1908; died March 22, aged 65, of coronary thrombosis.

William Allen Sinton, Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1925; member of the American Medical Association; served during World War II; affiliated with the Hospital for Women of Maryland, Maryland General Hospital and the Union Memorial Hospital, where he died January 20, aged 49, of hypertension and cardiovascular disease.

Mary E. Newman Sloan, Buffalo; University of Buffalo School of Medicine, 1900; member of the American Medical Association; died February 25, aged 73, of acute myocardial infarction.

George Arthur Smith, Long Hill, Conn.; Johns Hopkins University School of Medicine, Baltimore, 1907; member of the American Medical Association; served on the staffs of the Bridgeport and St. Vincent's hospitals in Bridgeport; died January 22, aged 70, of cerebral thrombosis.

Henry Slaymaker Smith, Shorewood, Wis.; Rush Medical College, Chicago, 1896; for many years medical examiner for the Northwestern Mutual Life Insurance Company; died February 17, aged 78, of carcinoma of the prostate.

Rufus Goldsmith Stanbrough, Floral Park, N. Y.; University of the City of New York Medical Department, 1875; died December 8, aged 96, of bronchitis and myocarditis.

William H. Townsend, Maplewood, Mo.; St. Louis College of Physicians and Surgeons, 1891; member of the American Medical Association; served as president of the Bank of Maplewood; died in the Missouri Baptist Hospital, St. Louis, February 24, aged 83, of cerebral thrombosis.

Howard H. Veon, Parkersburg, W. Va.; Ohio Medical University, Columbus, 1902; member of the American Medical Association; affiliated with Camden-Clark Memorial Hospital and St. Joseph's Hospital, where he died February 22, aged 70, after an operation for intestinal obstruction.

Herman Julius Von Lackum ✦ Dysart, Iowa; King Eclectic Medical College, Des Moines, 1886; served for many years on the board of education; bank director; died February 3, aged 88, of arteriosclerotic heart disease.

Harley Yandell, Springfield, Ill.; St. Louis University School of Medicine, 1911; died in Memorial Hospital February 22, aged 65, of cirrhosis of the liver and arteriosclerotic heart disease.

Foreign Letters

LONDON

(From a Regular Correspondent)

March 28, 1950.

Doctors in New Parliament

Ten doctors will sit in the new Parliament. Six are members of the Labour Party, three are Conservatives and one Liberal-Conservative.

LABOUR MEMBERS

Dr. A. D. D. Broughton (represents Batley and Morley) is 47, served five years in the Royal Air Force and first entered Parliament in February 1949.

Mr. Somerville Hastings (Barking) is 71, a retired ear, nose and throat surgeon, first sat in Parliament in 1923, a founder member of the Socialist Medical Association, member and chairman of the London County Council (the latter for 10 years) and is now an alderman.

Dr. S. W. Jeger (Holborn and St. Pancras South) is 51, is in general practice in London and has been on the London County Council since 1931. During the Spanish Civil War he visited Spain twice to give medical advice to Republicans, He was a founder member of the Socialist Medical Association. He was first elected to Parliament in 1945.

Dr. H. B. Morgan (Warrington) is 65, served in the 1914-1918 war and was in general practice 1921 to 1930. He has been an internist at Manor House Hospital (Trades Union) since 1931 and has held many posts in Trade Unions and the Trade Union Congress. He has been a Fabian since 1904. He was in Parliament 1929 to 1931, and has served since 1940. He has been a member of the Council of the British Medical Association since 1940.

Dr. Barnet Stross (Stoke-on-Trent Central) is 50 and was in general practice from 1925 to 1948. He was medical adviser to the North Staffordshire Miners Federation and Pottery Workers Society of Great Britain in 1927, councillor in 1937 and later alderman of city of Stoke-on-Trent. He entered Parliament in 1945. He founded the "Lidice shall live" organization in 1942. He was a member of the parliamentary delegation to Czechoslovakia in 1946 and was decorated by Mr. Jan Masaryk in 1947.

Dr. Edith Summerskill (Fulham West) is 49. She served on the Middlesex County Council from 1932 to 1938. She first became a member of Parliament in 1938. Since 1945 she has been Parliamentary Secretary to the Ministry of Food. She has always been concerned with questions relating to women and children and was invited by the Spanish government to examine conditions of women and children in Spain during the Civil War. She has examined public health conditions in many countries. She was the only woman to go in parliamentary delegation to Australia and New Zealand in 1944. She represented Great Britain at the Food and Agriculture Organizations' Conference at Washington in 1946 and Geneva in 1947. She is one of the organizers and vice president of the Socialist Medical Association. In January 1949 she became the first married woman (she has a son and daughter) to become a Privy Councillor.

CONSERVATIVE MEMBERS

Dr. R. F. B. Bennett (Gosport and Fareham) is 38 (qualified 1937). He served in the Royal Navy during the war and was twice torpedoed. He is credited with more than 500 flying hours as a pilot with Fleet Air Arm. He is a psychiatrist in South Hampshire. He represented England in the Olympic Games in 1936 and was on the British team which competed with Americans in 1949.

Mr. Walter Elliot (Kelvin-grove) qualified in 1913 (D.Sc., 1923). He has an honorary degree of LL.D. from the universities of Aberdeen, Edinburgh, Glasgow, Leeds and Manchester and a doctor of science from South Africa. He was Lord Rector of Aberdeen University 1933-1936, and is now Rector of Glasgow University. Elected a fellow of the Royal Society in 1935 and a fellow of the Royal College of Physicians in 1940. He served with the Medical Corps in World War I and was awarded the Military Cross and Bar. He was in Parliament 1918-1945 and has served since 1946. He became Privy Councillor in 1932. Since 1923 he has held the offices of Under-Secretary of Health for Scotland, Under-Secretary of State for Scotland, Financial Secretary to the Treasury, Minister of Agriculture and Fisheries, Secretary of State for Scotland and Minister of Health. He is well known through writings and broadcasting.

Col. Malcolm Stoddart-Scott (Ripon) is 49; he qualified in 1926 and held several intern appointments at Leeds General Infirmary. He served in the Medical Corps throughout World War II and was named an Officer of the British Empire in 1945. He has been honorary Secretary to the Conservative Parliamentary Health Committee and served on standing committees dealing with national health service, analgesia in childbirth, nurses, milk designation and others. He is chairman of the British Rheumatic Association. He first entered Parliament in 1945.

LIBERAL CONSERVATIVE MEMBER

Dr. Charles Hill (Luton) is 46 and secretary of the British Medical Association. He qualified in 1927. He was a London University extension lecturer and deputy medical officer of health for Oxford, became assistant secretary of the British Medical Association in 1932, deputy secretary in 1935 and secretary in 1944. He is a member of the Industrial Health Advisory Committee, Ministry of Labour, and Secretary of the Commonwealth Medical Conference. He has been active in the World Medical Association and is now president. He was formerly chairman and now is vice president of the Central Council for Health Education. He has broadcast for many years regularly for the British Broadcasting Company as the "Radio Doctor" and is the author of several books on health education. He enters Parliament for the first time.

BELGIUM

(From a Regular Correspondent)

LIÈGE, March 4, 1950.

Medicosocial Efforts at the Universities in Belgium

The Belgian Association of Social Medicine conducted a session to study the problems relating to the health of students. Interesting conclusions were reached at this session concerning the efforts which the four universities of the country have made for the students in the medicosocial sphere, particularly the prophylaxis of tuberculosis for students in Ghent. Since 1942, the students have been urged to submit to roentgenographic examination. In the five years which followed, 20 to 70 per cent of the students have been examined. Nevertheless, it is difficult to draw conclusions from these examinations. Some students suspected of having tuberculosis have not presented themselves for testing. During the year 1948-1949 the preventive examination was used systematically, and 92 per cent of those matriculated were examined (2,145 examinations). In 50 instances lesions were found among which there were about 40 cases of old or inactive lesions; there were 10 students with active tuberculosis among whom 7 were undergoing treatment and 3 had not known of their disease.

Other subjects were discussed. For example, a service of free meals for students of limited means was organized at the

time of the occupation; it has been successful since 1941. Twenty-six thousand meals were served in 1946. The problem of lodging also is important. A social committee of the student body is actively occupied with this matter and with the acquisition of books and facilities for studies. The expenses of study for a student who lives modestly are as high as 2,000 francs per month.

In Ghent the students have occasion to engage in sports: 20 per cent of the student population are active in competitive sports. Among the female students the percentage is the same. Medical supervision of sport activities exists, but it could be improved. From the point of view of sports the desire for superiority is not less than at the other universities, although at Liège sports activities have been affected by the destruction of the university's institute of physical education by bombing attacks.

Functional Visceral Enlargements of Nervous and Endocrine Origin

In the course of an extraordinary session of the Belgian Society of Gastroenterology in Brussels, Hillemand, Viguie and Woimant discussed functional visceral enlargements of nervous and endocrine origin. The authors called attention to the concurrence of these visceral enlargements with thyroid insufficiency. This association is found in drug addicts, and the disturbance does not always disappear with cure of the addiction, just as endocrine treatment does not always cause definite disappearance of disturbances caused by enlargement of an organ. There are also visceral enlargements secondary to disorders of the nervous system. Bensaude called attention to the disorder in postencephalitic paralysis agitans. Other authors have published similar cases of paralysis agitans.

The connection between the diencephalon and the hypophysis explains certain cases of visceral enlargement, and it is known that in the course of diseases of the spine, such as tuberculosis of the vertebrae, visceral enlargements are not exceptional. It is necessary to reserve a place for certain transitory visceral enlargements or those which develop after certain infectious diseases and which can be attributed to an encephalitis with involvement of neurovegetative centers. In order to make it possible to evaluate the frequency of visceral enlargements secondary to diseases of the central nervous system, systematic roentgenologic examination is advisable in all patients who present a diffuse involvement of this system.

Occupational Therapy in Dementia

At a special meeting of the Belgian Society of Mental Hygiene, Dr. Seghers stressed the therapeutic value of occupational therapy. The demonstration of cases at the Bethanie Institute in Antwerp convinced the members of the society of the results obtained thereby. Occupational therapy and collective gymnastic exercises or dancing were employed for patients with chronic mental illness and those with agitation, aggressiveness, impulsiveness, negativism, hallucinations and catatonia. Occupational therapy is a helpful adjunct to electroshock or shock treatment with insulin or pentamethylenetetrazol and to treatment with prolonged baths and hypnotics. It permits doing away with constraint and isolation in cells.

Illegal Medical Practice and Charlatanism

The development of various methods of quackery, which strive to circumvent laws, has made necessary the campaign started by the Belgium Society of Legal Medicine. This society has created a committee to study a motion which will be addressed to the public authorities. It will insist on measures regarded as indispensable in the fight against the illegal practice of medicine. At one of two sessions Hougardy took up the modern form of illegal practice and charlatanism in medicine.

One of the factors which hindered the campaign against quackery is the existence of "straw men," specious physicians. For dentists it has been possible to introduce into law dispositions permitting the condemnation of such persons, but when physicians are concerned there still seems to be hesitation. Other aspects of charlatanism include the medicopharmaceutic advertisements; although the Belgian radio has not encouraged it, the same cannot be said for broadcasts from neighboring countries. As regards the press, in spite of an effort at correction by several large newspapers, it still draws profit from advertisements for pharmaceutic products which often are of no value. Intensive propaganda by testimonials of patients making claims which are as astounding as they are unjustified is conducted. It is necessary to put restraint on this activity in the interest of the public as well as that of physicians.

Intestinal Bilharziasis in the Belgian Congo

At a meeting of the Belgian Society of Tropical Medicine, Janssen presented the results of an investigation made during two and a half years in the Belgian Congo on schistosomiasis, which is prevalent among the workers of the gold mines, affecting more than 85 per cent of the adult population. The nutritional conditions of the natives being satisfactory, he failed to reveal an insufficiency factor in the pathogenesis of the hepatic lesions which were observed. Biopsies of the liver gave a better insight into the nature of the lesions, and the author concluded that in the region of Tora at the border of the Haut-Ituri (Aruwimi) more than 80 per cent of the adult population are infected with Schistosoma mansoni. Two thirds of the patients have hepatomegaly.

The sulfobromophthalein sodium test of the liver proved of no value as an indicator of hepatic involvement. Analysis of the blood proteins did not lead to definite conclusions. Biopsies of the liver, according to the technic of Gillmann, provided evidence that the principal lesion consists of a chronic granular fatty degeneration around the ova. True sclerosis is rare.

Epidemic Myalgia

A disorder which is still little understood, and the appearance of which was first reported in Virginia in 1888 under the term "devil's grip," has received attention in Belgium. In 1942 L. van Bogaert observed a large number of cases of epidemic myalgia in the province of Antwerp. After his report to the Academy, the Health Service of Belgium alerted the medical corps of the country to the appearance of the new disease. Dr. Ronse published a monograph about it in *Bruxelles-médical* and indicated that epidemic myalgia is a disease characterized by painful muscular rigidity and apparently caused by a virus which attacks the meninges superficially. In certain cases the muscular or subcutaneous fascia shows characteristic nodular infiltrations. Sporadic cases are difficult to recognize; they appear in a latent form in various parts of the country.

Domus Medicorum

Numerous members of the Medical League long have recognized the necessity of creating a national organization of Belgian physicians which would centralize all associated services. With the cooperation of the professional organizations, of physicians' associations and of the laboratories of pharmaceutic products, this has become a reality. The numerous speeches given on this occasion stressed that medicine has the character of a liberal profession and as such it ought to develop, and, while in specialization it becomes more scientific, it should not cease to be an art and should not become a simple technic.

Professor de Beule

Professor de Beule of the faculty of medicine of Ghent died recently. He was one of the most brilliant and outstanding surgeons of this faculty. He was one of the first who resorted to surgical procedures on the nerves, and he presented a thesis on retrogasserian neurotomy for his doctorate.

De Beule exerted a great influence on Belgian surgery in the last thirty years. One of the older surgeons, Charles Willems, said of him with complete justification that for a number of years he was a master and a leader. He successively became president of the Belgian Society of Surgery, of the Belgian Society of Gastroenterology and, finally, of the Royal Academy of Medicine.

SPAIN

(From a Regular Correspondent)

MADRID, March 3, 1950.

Meeting of Society of Cardiology

The Society of Cardiology of Spain held its annual meeting, Dec. 3, 1949, in Madrid. Dr. L. Pescador of Madrid spoke on pericarditis. He reviewed clinical records in 8,500 cases, among which pericarditis was diagnosed clinically in 31 (0.36 per hundred cases). The incidental postmortem finding of pericardial scars in many cases is explained by the fact that a clinical diagnosis of pericarditis during the life of the patient is difficult to establish.

Experiments showed that certain reflexes originating in the visceral pericardium produce changes in the arterial blood pressure. A puncture of the visceral pericardium produces lowering of the arterial blood pressure, which does not occur if the visceral pericardium is anesthetized before puncture. Constant irritation of the visceral pericardium with iodine tincture produces permanent hypotension.

Clinically, pain is encountered in 80.6 per cent of the cases, dyspnea in 96.7 per cent, increased size of the liver in 98 per cent and an increased sedimentation rate in 100 per cent of the cases. In 4 fatal cases of pericarditis seen by the speaker, thrombosis of the veins of the right arm appeared in the course of the disease. This phenomena was previously described by Marañón.

The course of pericarditis has four main factors: inflammation, then formation of liquid, reabsorption and cure. In some cases the disease becomes cirrhotic in form and then evolves into constrictive pericarditis.

Rest, salt-free diet, mercurial diuretics, atropine and digitalis are of therapeutic value in the various stages of pericarditis. The speaker pointed out that the introduction of antibiotics into the pericardial sac is the route of selection. In 6 cases of tuberculous pericarditis, he administered streptomycin. Two of the patients were in advanced stages of the disease. The treatment failed. In the remaining 4 patients, a clinical cure was rapidly obtained. The patients have been observed for more than one year. There was no recurrence in 3 of the patients. In 1 patient the recurrence was controlled by administration of streptomycin the second time, and in 1 the administration of paraaminosalicyclic acid was a valuable adjuvant treatment.

There may be complete clinical cure in pericarditis. However, the speaker found that in patients clinically cured there is a systolic murmur over the pulmonary artery, which is of value for a retrospective diagnosis of pericarditis. Murmurs over the pulmonary artery have in the past been regarded as purely accidental murmurs.

When constrictive pericarditis develops, surgical treatment is necessary. The operation was successful in 1 of the 2 cases reported by the speaker.

The topic dealt with by Dr. Pescador was discussed by various cardiologists. In addition, Dr. Lozano of Sevilla spoke on constrictive chronic pericarditis, Dr. Estape of Barcelona on uremic pericarditis, Dr. Sánchez of Badajoz on spontaneous pneumopericarditis, Drs. Codina Altes and Juncadella of Barcelona on calcification of the pericardium, Dr. Bravo of San Sebastian on tuberculous pericarditis, Dr. Hernández of Madrid on rheumatic pericarditis and Dr. Caralps of Barcelona on surgical treatment of pericarditis (film).

SWEDEN

(From a Regular Correspondent)

STOCKHOLM, March 15, 1950.

Proposed Transfer of Austrian Doctors to Sweden

Austria and Sweden have approximately the same population, but, while there are about 12,000 doctors in the former, there are only about 4,500 in the latter. Last December the Swedish government decided to send a delegation of three, including Professor Lichtenstein, to Vienna and elsewhere in Austria to investigate the possibilities of large scale transfer of Austrian doctors to Sweden. This tour of inspection lasted from Jan. 10 to 23, 1950, and the report of the delegation to the Swedish government is now made public.

Much of this report is a comparative study of the medical curriculums in the two countries. It seems that the quality of the entrants to the study of medicine is more uniform in Sweden, where there are comparatively few students to each teacher and where the provision of quarters and textbooks is relatively satisfactory. In 1937 Vienna had 65 professors and "docents" in internal medicine alone. By 1939 this figure had been reduced to 19, and in 1945 it was 5. In Austria, clinical subjects are largely dealt with by lectures in "the old academic style," an exception being made with regard to the teaching of dermatology, which is carried out by demonstrations.

Sweden needs specialists in several branches of medicine, but the delegation found that Austria is at present so short of specialists that it has no surplus to export. But there is a surplus of comparatively young doctors, who are fairly well qualified according to the standard set in Sweden.

Complaints by Disgruntled Patients

The patient who feels neglected or ill treated by his doctor may appeal to a Disciplinary Committee, which submits the evidence on both sides to a careful scrutiny with the help of experts in the various branches of medicine concerned. After judgment has been given, details of such cases are published from time to time in the *Journal of the Swedish Medical Association.*

Infant Welfare Centers

In 1937 the Swedish Parliament voted funds for infant welfare centers. In 1947, 87 per cent of all the country's infants had come into this scheme. Dr. Fritz Karlström of Karlstad has made a statistical study of conditions in the County of Värmland. A hospital in this county receives most of the children requiring medical treatment, and it is therefore able to provide figures showing the incidence of certain diseases as they affected children who had been in touch with infant welfare centers.

There are, of course, many pitfalls in such a comparison. Dr. Karlström has chosen the following diseases for his comparison: rickets and spasmophilia, acute diseases of the respiratory tract, acute diarrhea and anemia. In the five year period 1944-1948, a total of 23,450 babies were born in the county, and 21,789 of them were registered in an infant welfare center. The incidence of rickets and spasmophilia was ten times greater among the infants not thus registered than among those who were. A similar but less marked difference was observed with regard to the other diseases, and, when all four groups of diseases were grouped together, their frequency was four times greater among the infants not registered than among those who were. The death rate was about seven times as high among the former as among the latter. Breast feeding was twice as common among the infants attending welfare centers as among the controls.

BRAZIL

(From a Regular Correspondent)

Rio de Janeiro, Feb. 20, 1950.

Studies on Rickets in Porto Alegre

Dr. Stella Budiansky, of the University of Porto Alegre department of pediatrics, reported recently the results of her studies of rickets in 295 children 5 years of age and under during 1947 and 1948 in Porto Alegre, a community of 400,000 population in Rio Grande do Sul. The large majority of her cases were not of florid or major rickets, common in Europe and North America, but of discrete or minor rickets, which has been described for several years in Central and South America. Rickets is scientifically and statistically significant, with respect to morbidity and mortality of very young children. The 295 children were of families of poor socioeconomic status, living in a block of low rent houses administered by the Legião Brasileira de Assistencia, a semigovernmental welfare organization. The children were divided into two groups, 151 children of less than 2 years of age in the first group and 144 from 2 to 5 years in the second. The annual total of sunshine hours averages 2,303 in Porto Alegre (Montevideo, Uruguay, has 2,571, and Buenos Aires, Argentina, has 2,396), but in 1947 and 1948, the years during which Dr. Budiansky's investigations took place, the total annual sunshine hours were 2,658 and 2,479, respectively. For each child the clinical signs of rickets, radiologic changes of the bones, determinations of the bone age, statural age and blood phosphorus and phosphatase were investigated.

In the 295 children, 31 cases (10.51 per cent) of clinical rickets were found, in 12 (4.07 per cent) of which there were radiologically positive observations. Thirty of the 31 cases were in the first group (19.86 per cent), 11 (7.28 per cent) of which were radiologically positive. The only case (0.7 per cent) of rickets in the second group was proved clinically and radiologically. In these mild cases there were slight clinical, radiologic and/or humoral manifestations. Even in the rare cases of the severe type of the disease, identical with those described in Europe and the United States, high phosphatase levels were not observed. The highest level found in Dr. Budiansky's patients was 47.5 King-Armstrong units, which occurred in the severest case with serious lesions evidenced clinically and radiologically. In normal children the phosphatase level varied between 3.81 and 10.89 units. There was a higher incidence of the disease in male and in Negro children, but breast-fed and syphilitic children did not show a higher incidence than bottle-fed and nonsyphilitic children. The author points out that rickets, even in this mild form, is an important contributing cause of morbidity and mortality: during the two year investigation 11 children died in the 0-2 year age group, 6 among the 30 rachitic children (20.0 per cent) and 5 among the 121 nonrachitic children (4.13 per cent).

Meeting of Brazilian Hematologists

The first Congress of the Brazilian Society of Hematology and Hemotherapy will be held at Rio de Janeiro on May 21-26. The organizing committee is composed of Drs. W. Oswaldo Cruz, Heraldo Maciel, Arthur Cavalcanti, João M. Mendonça and P. Clovis Junqueira, of Rio de Janeiro; Carlos Lacaz, Oswaldo Mallone, Michel A. Jamra, F. Ottensooner and Ruy Faria of São Paulo; Menandro Novais of Bahia; Carlos E. Frimm of Rio Grande do Sul and Cortes Villela of Minas Gerais. Among the subjects to be discussed at the meeting are the treatment of leukopathies, treatment of the anemias, immunohematology, medicosocial study of blood donors and preservation of blood and its derivatives. Dr. João M. Mendonça (31 rua Mexico, Rio de Janeiro) is in charge of the Congress' office.

Social Factors and Health

The Center of Studies of Social Medicine is promoting a meeting to be held at the Academia Nacional de Medicina March 20-25, to discuss the most important social measures aiming at the protection of human health. The following subjects will be presented for discussion: Mixing of Human Races (Dr. A. Austregesilo), Juvenile Delinquency (Dr. Roberto Lira), Syphilis (Dr. Demetrio Peryassú), Social Factors in Tuberculosis (Dr. Zey Bueno), Alcoholism (Dr. Mauricio de Medeiros), Eugenics and Crime (Dr. Spinosa Rothier), Social Aspects of Crime (Dr. Nelson Hungria), The Human Factor in Traffic Accidents (Dr. José Kritz), Pauperism and Undernutrition (Dr. Cumplido de Sant'Anna) and City Slums (Dr. C. de Lacerda).

ARGENTINA

(From a Regular Correspondent)

Buenos Aires, March 7, 1950.

New Medical Schools

The Medical School of the University of Tucumán (recently established) will open this year. The University of Cuyo is planning the establishment of a medical school in Mendoza, at the foot of the highest Andes mountain. There are at present in full activity, four medical schools in Argentina: Buenos Aires, Córdoba, Rosario and La Plata. There are no private medical schools. Recently it has been stated that all university students should present at matriculation a certificate of "good behavior" granted by the federal police. This certificate is not always granted to persons who have expressed political ideas contrary to those of the national authorities.

Ministry of Public Health

The Ministry of Public Health has greatly increased its organization. Many new departments have been established and a great number of persons employed, with expensive budgets. Persons working in government public health institutions must attend public official meetings; severe measures will be applied to those who do not attend. Hygiene and educational medicine will become a branch of the Ministry of Public Health instead of the Ministry of Education.

Vitamin A in Premenstrual Tension

Drs. J. Argonz and C. Abinzano of the Endocrinological Service of the Rivadavia Hospital (under the direction of Prof. E. B. del Castillo) have obtained successful results in 100 cases of premenstrual tension treated with vitamin A. Complete relief of mastodynia was effected. Abdominal pains decreased. Edema, lumbar pains and nervous symptoms were not observed. The improvement of mammary disturbances was remarkable. A daily dose of 200,000 units is given orally during the second half of the cycle. The medication must be repeated for four or five consecutive monthly periods in order to obtain a prolonged result. Results are not so satisfactory with smaller doses or shorter periods.

Enrique and Ricardo Finochietto Foundation

Dr. Ricardo Finochietto has established a foundation in memory of his brother, Dr. Enrique Finochietto, the most renowned surgeon in this country. Dr. Ricardo Finochietto and a large number of the most outstanding surgeons in Argentina have been trained under his direction. The initial fund of the foundation is one million argentine pesos and the principal aims are to assist and stimulate the advancement of medicine in and out of the country.

Personal

Dr. Abelardo Irigoyen Freire, former Ministry of Sanity in the Province of Santa Fé, died recently of uremia. He was 45 years old.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part II.* Various medical schools, April 24-25. *Parts I and II.* Various locations, June 19-21. Final date for accepting applications is May 19. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th Street, Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations. July 21. *Oral.* Philadelphia, April 23-27, Chicago, Oct. 8-11. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* San Francisco, June 21-23. The oral examinations in the subspecialties will be held at the same time and places. *Written.* Oct. 16. Final date for acceptance of applications is May 1. Asst. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Applications no longer accepted. Chicago, Oct. 1950. Final date for filing applications is April 30. Sec., Dr. W. J. German, 789 Howard Ave., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Oral Part II.* Atlantic City, May 21-27. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* New York, April 21-22; Atlanta, April 28-29; Indianapolis, April 28-29; Denver, May 5-6. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1951. Final date for filing applications is July 1, 1950. *Practical.* Boston, May 22-26; Chicago, Oct. 2-6; West Coast, Jan. 1951. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* San Francisco, May. Chicago, October. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: Cincinnati, May 5-7; San Francisco, June 30-July 2. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* Boston, Aug. 26-27. Final date for filing applications is April 1. Sec., Dr. Robert L. Bennett, 30 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral.* May-June. Sec., Dr. Louis T. Byars, 4647 Pershing Avenue, St. Louis, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: *Written.* Portland, Ore., May 28. *Oral.* Portland, Ore., May 29. Sec., Dr. E. L. Stebbins, 615 N. Wolfe St., Baltimore 5, Md.

AMERICAN BOARD OF PROCTOLOGY: *Part I.* San Francisco, Dallas, Minneapolis and Philadelphia, May 13. Sec.-Gen., Dr. Louis A. Buie, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: San Francisco, June 23-24. Applications no longer accepted. Next examination, December 1950. Final date for filing applications is Sept. 1.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, week of June 18. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various centers, Oct. 25. Final date for filing applications is July 1. Sec., Dr. J. Stewart Rodman, 225 South 15th Street, Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 10-14, 1951. Final date for filing applications is Sept. 1, 1950. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 21.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ARKANSAS: * *Examination.* Little Rock, June 8-9. Sec., Dr. Joe Verser, Harrisburg. Homeopathic. Little Rock, June and November. Sec., Dr. Carl S. Bungart, 105 N. 14th St., Fort Smith. *Eclectic.* Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main Street, Little Rock.

CALIFORNIA: *Examination, Written.* San Francisco, June 19-22; Los Angeles, Aug. 21-24; Sacramento, Oct. 16-19. *Examination, Oral and Clinical for Foreign Medical School Graduates.* San Francisco, June 18; Los Angeles, Aug. 20; San Francisco, Nov. 12. *Reciprocity, Oral Examination.* San Francisco, June 17; Los Angeles, Aug. 19; San Francisco, Nov. 11. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

CONNECTICUT: * *Examination.* Hartford, July 11-12. Sec. to the Board, Dr. Creighton Barker, 160 St. Ronan St., New Haven. *Homeopathic.* Derby, July 11-12. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: *Examination.* Dover, July 11-13. *Reciprocity.* Dover, July 20. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Examination.* Washington, May 8-9. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington 1.

FLORIDA: * Jacksonville, June 25-27. Sec. Dr. Frank D. Gray, 12 N. Rosalind Avenue, Orlando.

GEORGIA: *Examination.* Atlanta and Augusta, June. *Endorsement.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

HAWAII: *Examination.* Honolulu, July 10-13. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, July 10. Sec., Mr. Armand L. Bird, 305 Sun Bldg Boise.

INDIANA: *Examination.* Indianapolis, June. Sec., Dr. Paul R. Tindall 1138 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Iowa City, June 12-14. Sec., Dr. M. A Royal, 506 Fleming Building, Des Moines 19.

KANSAS: Kansas City, June 7-8. Sec., Dr. J. F. Hassig, 905 N 7th Street, Kansas City.

KENTUCKY: *Examination.* Louisville, June 14-16. Sec., Dr. Bruce Underwood, 620 S. 3rd Street, Louisville 2.

MAINE: *Examination and Reciprocity.* Augusta, July 11-12. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, June 20-23. Sec. Dr. Lewis P. Gundry, 1215 Cathedral Street, Baltimore 1, *Homeopathic.* Baltimore. June 20-21. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: *Examination.* Boston, July 11-14. Sec., Dr. George L. Schadt, Room 37, State House, Boston 33.

MISSOURI: Examination. St. Louis, May 31-June 2 and June 7-9 Exec. Sec., Mr. John A. Hailey, Box 4, State Capitol Building, St. Louis.

NEBRASKA: * *Examination.* Omaha, June 5-7. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Building Lincoln 9.

NEVADA: Carson City, May 1. Sec., Dr. George H. Ross, 112 Curry Street, Carson City.

NEW HAMPSHIRE: Concord, Sept. 13. Sec., Dr. John Samuel Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 20-23. Sec., Dr. E. S Hallinger, 28 West State Street, Trenton.

NEW YORK: *Examination.* Albany, Buffalo, New York and Syracuse. June 27-30. Sec., Dr. Jacob L. Lochner, Jr., 23 S. Pearl St., Albany.

NORTH CAROLINA: *Endorsement.* Pinehurst, May 1. *Written* Raleigh, June 19-22. *Endorsement.* Raleigh, June 19. Sec., Dr. Ivan Procter, 226 Hillsboro Street, Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 5-7. *Reciprocity* Grand Forks, July 8. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 14-17. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr Clinton Gallaher, 813 Braniff Building, Oklahoma City.

OREGON: *Endorsement.* Portland, April 28-29. *Written.* Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Building, Portland 4.

SOUTH CAROLINA: *Examination.* Columbia, June 26-29. *Reciprocity* First Monday of each month. Sec., Dr. N. B. Heyward, 1329 Blanding Street, Columbia.

SOUTH DAKOTA: * Sioux Falls, July 18-19. Sec., Dr. C. E. Sherwood, 300 First National Bank Bldg., Sioux Falls.

TEXAS: * *Examination.* Austin, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination.* Salt Lake City, June. Dir., Dr. Frank E. Lees, 324 State Capitol Building, Salt Lake City.

VIRGINIA: *Examination.* Richmond, June 23-24. *Endorsement.* Richmond, June 22. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WISCONSIN: * Milwaukee, July 11-13. Sec., Dr. C. A. Dawson, River Falls.

WYOMING: *Examination.* Cheyenne, June 5. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 9. Sec., Mr. L. E. Gebauer, 1002 Donaghey Building, Little Rock.

CONNECTICUT. *Examination.* New Haven, June 10. Exec. Asst., State Board of Healing Arts, M. G. Reynolds, 110 Whitney Ave., New Haven.

FLORIDA: *Examination.* Gainesville, June 3. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

MICHIGAN: *Examination.* Detroit and Ann Arbor, May 12-13. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

NEBRASKA: *Examination.* Omaha, May 2-3. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, June 17. Sec., Dr. C. D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: *Examination.* Providence, May 10. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Vermillion, June 2-3. Sec., Dr. Gregg M. Evans, 310 E. 15th Street, Yankton.

Medical Motion Pictures

REVISED EDITION OF MOTION PICTURE REVIEWS NOW AVAILABLE

The Committee on Medical Motion Pictures has completed the second revised edition of the booklet entitled "Reviews of Medical Motion Pictures." This booklet now contains 225 reviews of medical and health films reviewed in THE JOURNAL to Jan. 1, 1950. Each film has been indexed according to subject matter. The purpose of these reviews is to provide a brief description and an evaluation of motion pictures which are available to the medical profession. Each film is reviewed by competent authorities. Copies are available at a cost of 25 cents from: Order Department, American Medical Association, 535 North Dearborn Street, Chicago 10.

FILM REVIEWS

Allergy, Immunology, Diagnosis and Treatment. 16 mm., color, sound, showing time fifty-three minutes. Directed by Leo H. Criep, M.D., Associate Professor of Medicine, Department of Immunology and Medicine, University of Pittsburgh and the Montefiore Hospital, Pittsburgh. Produced in 1949 by the Medical Film Guild under a grant from Wyeth, Incorporated, Philadelphia and Nepera Chemical Company, Inc., Nepera Park, Yonkers, N. Y. Procurable on loan from Wyeth, Incorporated, Film Library, 1600 Arch Street, Philadelphia 3.

The film discusses the immunologic principles of allergy and their application to the management of allergic manifestations. It appears to be intended to cover the entire field of allergy, and the script often is dogmatic and presents but one side of controversial subjects. To the student and general practitioner unfamiliar with the field, it would appear that such presentations are fact rather than theory. For example, one hears the following theories and personal beliefs as expressed as finalities: Histamine is the cause of the allergic reaction; the union of antigen and antibody is due to attraction of opposite electrical charges; 18 intradermal tests are done at a sitting; the tests are read in 10 minutes, and allergy (instead of heightened sensitivity) to physical agents. In describing the preparation of extracts the impression given is that there is only one procedure that can be followed. This is misleading, and one may seriously question the wisdom of presenting this phase of the subject in a film of this type. One of the most pertinent criticisms of the film is the repeated and obvious commercial references.

The film should be suitable for general practitioners and perhaps medical students, provided the audience is given sufficient explanatory data and additional information. In general the photography is satisfactory. Many photomicrographs are poor and consequently are not instructive. The animation and narration are excellent. With the exception of these criticisms, the teaching material is generally authentic and well coordinated.

You Can Hear Again. 16 mm., black and white, sound, showing time twenty minutes. Prepared and produced in 1949 by the Department of Medicine and Surgery, Veterans Administration. Procurable on loan from Chief, Medical Illustration Division Research and Education Service, Veterans Administration, Washington, D. C.

This motion picture vividly portrays, in a series of well photographed sequences, the effects on the economic and social life within a family when one of the members suffers serious impairment of hearing. The extent of the services offered by government agencies to veterans, the tests used for scoring the hearing loss and the procedures used in selecting a hearing aid, teaching the patient how to use it and helping to conserve his speech are well depicted. A technical difficulty arises in the attempt to suggest the loss of fidelity in the patient's hearing; unfortunately, the low fidelity of the sound-reproducing mechanism itself stands in the way of bringing out any subtle changes in the patient's perception of sound.

The film as a whole has the peculiar air of propaganda. The idyllic scenes in which the newcomer is welcomed with a handshake and called "Harry" would strike some audiences as misleading but must be interpreted in terms of the purpose of the film and the groups for whom it is intended. It will probably be most useful for showing to deafened veterans who need to be oriented toward the program that has been set up for their rehabilitation and to hospital personnel who are being trained for participation in this work.

Esophagogastrostomy for Achalasia of the Esophagus. 16 mm., color, sound, showing time twenty-four minutes. Prepared in 1949 by John L. Madden, M.D., St. Clare's Hospital, Department of Surgery, New York. Produced by and procurable on rental or purchase from Sturgis-Grant Productions, Inc., 314 East Forty-Sixth Street, New York 17.

This motion picture shows briefly the indications for surgical intervention in the treatment of achalasia of the esophagus, demonstrating diagrammatically the purpose of the operation. It proceeds quickly to the actual surgery in the case depicted.

The left lobe of the liver is elevated and the distal esophagus is mobilized to obtain adequate exposure. It demonstrates the development of the consecutive steps in the construction of the new opening between the lateral aspect of the distal esophagus and the fundus of the stomach. The patient is shown postoperatively taking a light meal, which would not necessarily be conclusive that operation had accomplished an appreciable change in the swallowing function.

The film is excellent in its surgical aspects. There is no mention of the part played by conservative therapy in these cases; it appears to be inferred that the patient comes directly to surgery when the diagnosis has been made.

This production can be recommended for state medical society meetings, general surgeons, and residents and interns on surgical services. The photography and narration are excellent.

Bureau of Medical Economic Research

MEDICAL ECONOMIC REVIEWS AND ABSTRACTS

Prepared by the Staff of the Bureau of Medical Economic Research

The Moral of the British Crisis.. By Sir Hubert Henderson. *The Review of Economics and Statistics* **31**: 256 (Nov.) 1949.

Policies of a welfare state cannot be expanded with total disregard to the economic resources and limitations of a nation. This theme was advanced in a recent article by Ffrangcon Roberts, a British physician (Where Are We Going? Medicine in a Planned Economy, *Brit. M. J.* [March 13] 1948; reviewed in THE JOURNAL, July 30, 1949); it is noteworthy that Sir Hubert Henderson, a professor of political science at Oxford, should independently reiterate the same point while concerning himself with the present economic crisis in Great Britain.

Sir Hubert's paper confines itself to a succinct statement about the British policy of handling its present financial crisis. The disadvantageous balance of payments, or what is more manifest, the alarming decrease in the British gold and dollar reserves, is familiar to most readers. The past war has resulted in such a destruction of British capital that the English people have found it necessary to borrow—more basically, to consume more than they produce—in order to maintain a partial semblance of their prewar living standards. The optimism that was evidenced in the early part of the past year over British recovery was "ridiculously premature"; the balance in international payments that seemed evident at that time hinged on temporary circumstances and the inclusion of Marshall plan aid in their computation. The American "recession," popularly blamed by some as the chief source of Britain's troubles, is quickly dismissed with the following quotation from the London *Economist:* "If British socialism cannot adapt itself to as minor a quaver as this, then it is too delicate for the real world" (page 256).

The pressure on the British to reduce costs in order to compete in a world market is obvious to the author. With the disappearance of a sellers' market, however, a reduction in price (cost) of British goods will not necessarily mean an increased

volume of sales and presumably a favorable (or less unfavorable) balance of trade. The all-important goal is the preservation of Britain's remaining dollar balance; to Sir Hubert a restriction in dollar imports is indispensable. He is likewise adamant in his view that this should be accomplished through import restrictions. The failure of the labor government to control the balance of payments is not prima-facie reason for reverting to a "free," or "price-system," market to remedy the situation. Under present "austerity" the demand for goods is becoming inelastic and higher prices will not be met with proportionally reduced buying and importing.

Import restrictions, on the other hand, will have the adverse result of aggravating the price disparity between British and American goods. The immediate remedy for this is devaluation. (Sir Hubert's article was written in July 1949, before the British devaluation in September 1949.) Devaluation, however, is valueless if there should result proportional increases in wages and sterling costs in Britain. In fact, such rises would be inevitable unless rigid controls were exercised over wages and prices. Henderson's stand is basically sound economics, if not sound politics; the inflationary trend must be stopped if any devaluation procedures are adopted.

But why does inflation continue?

"It is here that we reach what is really wrong in the economic policy that has been pursued in Great Britain in recent years. The main cause of our continuing inflation is undoubtedly, in my opinion, the growth of public expenditure, partly on defense, partly on food subsidies, and partly on the expansion of social services. During the past year, the total of our budgetary expenditure on these purposes has increased at a formidable rate, and it is still increasing. This, in my judgment, is mainly responsible for the fact that inflation still continues in Great Britain, though it has been arrested in many European countries. . . . There has been no greater practical fallacy than the idea which has been so fashionable in Britain in recent years that the balance between expenditure and revenue is all that matters, and that the counter-inflationary influence of financial policy can be reduced to terms of a simple subtraction sum" (page 258).

It is Sir Hubert's position that public expenditures, even if offset through taxation, are still inflationary. The taxes are "paid" through reduced savings rather than reduced expenditures; persons will reduce savings before they will reduce what they customarily expect as a standard of living. The effect of taxation in curtailing demand, claims Sir Hubert, cannot be rated at more than a fraction of the revenue raised.

"On the other hand, the addition to the demand for goods and services resulting from an increase in budgetary expenditure must be equivalent to the greater part, probably to about three-quarters, of that increase. Expenditure on the health service, which is today perhaps the most lavish feature in our national life, is peculiarly inflationary in its effect" (page 258).

While the British medical scheme results in some persons' paying more in taxes to support it than others, the latter will be more disposed to increase their personal expenditures than the former would be to cut theirs, with the inevitable inflationary results. To this strain on Britain's limited productive resources must be added the impact on the dollar balance of such items as lenses to meet the demand for spectacles.

Increasing productivity provides, as Sir Hubert says, a "margin for new social reforms," but the social services in Britain have been expanded with such fervor as to outstrip this increment and to leave no margin to meet the expanding needs for defense.

Britain's crisis is not conditioned by its reliance on physical rather than price controls:

"Our fault is the much simpler and more serious one of persisting as a people in trying to live above our means; and for this it is not administrative waste, but the pressing forward of the policy of the welfare state, without regard to economic or financial limitations, that is chiefly responsible" (page 260).

A postscript by the author in September 1949 states his inability to note any effort to halt the tide of inflation. The excesses are maintained in the name "full employment," their control attempted through "appeals" and "threats." He expects further crises in the British economy.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Resident's Liability for Negligence of Operating Surgeon. — The plaintiff sued for damages caused by the alleged malpractice of the defendant physician. From a judgment in favor of the plaintiff the defendant appealed to the district court of appeal, second district, division 1, California.

The plaintiff had been advised by Dr. Percy that an enlarged gland in the axilla should be removed and examined microscopically to determine whether it was malignant. The plaintiff accepted this advice and entered the hospital, signing the usual form consenting to such operations as might be "deemed advisable or necessary." The gland was removed and sent to the hospital laboratory for an analysis. While the plaintiff was still under anesthesia, the head nurse announced that the laboratory finding was carcinoma. The decision was then made—by whom it was made was a matter of dispute—to proceed at once and remove the plaintiff's right breast. This operation was performed. However, just prior to the plaintiff's removal from the operating room after completion of the operation, the laboratory announced that it had made a mistake in its diagnosis and that the laboratory then thought the condition was "Hodgkin's disease or a possible lymphoma."

The defendant was a resident physician at County General Hospital assigned to the surgical services of which Dr. Percy (who died prior to this trial) was chief, and it was his duty to assist Dr. Percy as directed. Except as assistant to Dr. Percy, the defendant had no connection with plaintiff's case or her operation. Although Dr. Percy had directed the defendant to perform the operation, Dr. Percy himself had done a great deal of assisting and had performed certain difficult parts of the operation alone. The defendant argued that the evidence was insufficient to find him negligent. He claimed that Dr. Percy was in charge of the case and, because he was assigned to assist Dr. Percy in the operation, it was his duty to follow directions given him during the conduct of the operation.

The most that the record indicates, said the court, is that, owing to a mistaken report emanating from the hospital laboratory and relied on by Dr. Percy, who was in charge of the plaintiff's case, Dr. Percy, assisted by the defendant who acted entirely under the direction of Dr. Percy, removed the plaintiff's breast during the time elapsing between the erroneous carcinoma report and the later corrected report showing that such condition did not exist. This is far short of the required substantial evidence necessary to support a judgment against the defendant.

It requires no argument and no citation of authorities, continued the court, to sustain the proposition that defendant cannot be held liable for malpractice in reference to the plaintiff's operation unless there is proof of some wrongful or negligent act on his part. That a most lamentable error occurred, resulting in serious injury to the plaintiff, cannot be denied. Such fact, however, affords no excuse for penalizing the defendant in the absence of evidence of fault. It must be remembered that the defendant was not the surgeon in charge of the operation, but a mere assistant. The record discloses no evidence that the defendant made any decision as to how soon the operation should be performed, and it is a reasonable conclusion that this matter, as indeed all matters connected with the operation, were decided by the surgeon in charge, Dr. Percy. Hence, assuming but not deciding that there was "negligent haste," such fault cannot be charged to the defendant.

In like manner any "negligent and mistaken diagnosis," the causa causans of the plaintiff's injury, was a matter with which defendant had no connection whatever. The mistake in question emanated from the pathologic laboratory of the hospital, which at a previous trial of the case was absolved from liability.

Judgment in favor of the plaintiff was therefore reversed. — *Valdez v. Hankins, 211 P. (2d) 6 (Calif., 1949).*

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodical are available from 1939 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

38:641-800 (Nov.) 1949

*Calcification as Diagnostic Sign of Syphilitic Aortitis. M. C. Thorner, R. A. Carter and G. C. Griffith.—p. 641.

*Biomicroscopy of Conjunctival Vessels in Hypertension: Capillary "Hypertension Pattern" and Occurrence of Intravascular Clumping (Sludged Blood) are Described. A. Lack, W. Adolph, W. Ralston and others.—p. 654.

Normal Unipolar Precordial and Limb Lead Electrocardiogram. M. Sokolow and R. D. Friedlander.—p. 665.

Heart Muscle and Electrocardiogram in Coronary Disease: II. Difficulties of Description and Illustration of Ventricular Muscle Lesions, with Method for Their Graphic Representation in Myocardial Map. J. J. Sayen and W. F. Sheldon.—p. 688.

Occurrence of Paroxysmal Hypertension in Patients with Intermittent Claudication. M. R. Malinow, B. Moia, E. Otero and M. Rosenbaum. —p. 702.

Role of Anemia in Experimental Production of Heart Block and Auricular Fibrillation in Dog. L. Horlick and A. Surtshin.—p. 716.

Influence of Vagal Activity on Heart Block: Study of Effect of Oxygen, Mecholyl, and Atropine on Auriculoventricular Conduction Time. A. L. Messer, C. K. Donegan and E. S. Orgain.—p. 732.

Relationship of Dicumarol Absorption to Gastric Free Hydrochloric Acid. S. R. LaTona and F. LeFevre.—p. 743.

Calcification as Diagnostic Sign of Syphilitic Aortitis.—Thorner and his associates observed calcifications of the ascending aorta alone, or with calcification of the knob, with sufficient regularity in cases of syphilitic aortitis studied roentgenologically to stimulate their interest in its significance. They felt that demonstration of calcification in the different portions of the aorta should be of value in the differential diagnosis of these two conditions. They reviewed all cases of syphilitic aortitis that came to autopsy at the Los Angeles County General Hospital from December 1938 to July 1947. Of a total of 400 cases, roentgenograms of 122 patients taken prior to death were available for examination. Eight hundred and one autopsied cases of atherosclerosis of the aorta of the same period were studied until 100 cases with available roentgenograms were collected. Of the 122 cases of syphilitic aortitis, 22 showed calcification of the ascending aorta, as compared with 2 of the 100 cases of atherosclerosis of the aorta. The authors were able to demonstrate the difference in sites of deposition of calcium in the thoracic aorta in syphilis and arteriosclerosis. The youngest patient in the nonsyphilitic group was a 60 year old man; the average age was 72.7 years. In the syphilitic group the youngest age represented was 32 years and the average age was 58 years. Syphilis is usually acquired early in life, and, therefore, in spite of the fact that the average duration of the disease in patients showing calcification was 34.6 years, calcification was found earlier in life in syphilitic patients than in the arteriosclerotic group. Linear calcification of the ascending aorta in patients under 60 years of age is usually due to syphilitic aortitis. Calcification of the ascending aorta is evidence of late, relatively inactive syphilis. Calcification of the ascending aorta is a valuable aid in the differential diagnosis of the etiology of aortic insufficiency and in distinguishing aneurysms from neoplasms.

Biomicroscopy of Conjunctival Vessels in Hypertension.—Lack and his co-workers feel that the role played by capillaries in hypertension has received inadequate clinical study and definition. Utilizing recent advances contributed by studies of living circulation in animals, the authors found an adaptation of the basic technics applicable to patients. They observed the conjunctival vessels overlying the sclera of the eye by reflecting bright parallel beams of light off the sclera. The images of the conjunctival vascular tree were studied by direct microscopy. An ophthalmologic slit lamp apparatus provided support for the patient's head and a maneuverable light source. A compound microscope was mounted on a horizontal rack and pinion; 16 and 24 mm. objectives provided safe working distances. Magnifications up to 200 times were used. Repeated examinations of patients made it possible to study changes in the peripheral vessels. Two control series were concurrently studied: a hospital group of 64 normotensive patients and a group of 50 normal adults. Biomicroscopy studies were made also on 100 patients with hypertension. A "hypertension pattern" of capillary changes was noted. This pattern is characterized by narrowing, elongation and looping of capillaries, which, in addition, show fixed angularities or tortuosities, tubular thickening of walls and loss of normal distensibility. Ninety-eight per cent of all hypertensive patients showed significant capillary changes of this type. The severity of this capillary hypertension pattern correlated directly with the rise in diastolic pressure. Arteriolar pathologic changes were noted in 80 per cent of the hypertension series. Nonhypertensive hospital patients showed no capillary involvement in 72 per cent. Minimal changes of bizarre types were present in 28 per cent; none showed the "hypertension pattern." Intravascular clumping of red cells was noted in 96 per cent of the hypertension series and in 67 per cent of the control series. These findings indicate the value of study of the capillaries in hypertension.

American Journal of Ophthalmology, Chicago

32:1631-1776 (Dec.) 1949

*Retrolental Fibroplasia in Premature Infants: II. Studies on Prophylaxis of Disease: Use of Alpha Tocopheryl Acetate. W. C. Owens and E. U. Owens.—p. 1631.

Physiology of Intraocular Fluids and Its Clinical Significance. S. Duke-Elder.—p. 1638.

Circulatory Aspects of Glaucoma Problem: Second Mark. J. Schoenberg Memorial Lecture. J. N. Evans.—p. 1645.

Glomus Cells in Human Choroid as Basis of Arteriovenous Anastomoses. A. Loewenstein.—p. 1651.

Panophthalmitis Caused by Escherichia Coli Communior. R. J. Nicholl and D. Locatcher-Khorazo.—p. 1660.

Intraorbital Meningiomas: Clinicopathologic Study. W. McK. Craig and L. J. Gogela.—p. 1663.

True Psychosensory Dilation and Delayed Psychosensory Dilation of Pupil: Preliminary Report. N. S. Jaffe.—p. 1681.

Experimental Studies on Sympathetic Ophthalmia. R. C. Collins. —p. 1687.

Detachment of Anterior Layers of Iris (Iridoschisis): Report of Case. J. G. Linn and J. G. Linn Jr.—p. 1700.

Correlation of Microscopic and Slitlamp Examinations of Developing Hereditary Cataracts in Mice. G. K. Smelser and L. von Sallmann. —p. 1703.

Cyclodialysis: I. Discussion of Techniques. O. S. Lee and J. H. Allen. —p. 1713.

Aniseikonia for Distant and Near Vision. K. N. Ogle and W. Triller. —p. 1719.

Enucleation and Allied Procedures: Part II. Survey of Semiburied Implants. J. S. Guyton.—p. 1725.

Nonsurgical Treatment of Heterotropia. R. G. Scobee.—p. 1734.

Retrolental Fibroplasia in Premature Infants: Use of Alphatocopherol Acetate.—Owens and Owens point out that there are considerable differences of opinion as to the nature and origin of the membrane behind the lens. The main reason for these differences arose from the fact that the earlier reports had been limited to examinations made when the disease was well advanced. They had demonstrated that retrolental fibroplasia starts in the retina in postnatal life. They describe observations on the eyes of 101 premature infants with birth weights of 1,360 Gm. (3 pounds) or less, who were examined at definite intervals from the date of birth. The earliest detectable change, occurring three to five weeks after birth, was a dilatation of the retinal veins and an increased tortuosity of the retinal arteries. The retina became grayish-green and swollen. The vitreous became cloudy, and proliferating fibrous bands extended forward from the elevated retina into the vitreous. The retrolental membrane was formed by the fusion of the vitreous bands and the peripheral folds of swollen elevated retina. These authors point out that the diet recommended for premature infants contains little of the fat-soluble

vitamins. Since a deficiency in vitamin E seemed likely, alternate premature infants admitted to the Johns Hopkins Hospital were given supplements of *dl*-alphatocopherol acetate, 50 mg. every eight hours. In only 1 of the 23 infants who received these supplements did retrolental fibroplasia develop, whereas it occurred in 17 of 78 infants who did not receive vitamin E supplements.

American Journal of Surgery, New York

78:801-930 (Dec.) 1949

*Meckel's Diverticulum: Review of 39 Cases. G. P. Schwei and A. S. Jackson.—p. 804.
Development of Total Pneumonectomy. R. Nissen.—p. 816.
Inquiry into Late Postpartum Hemorrhage. G. F. Melody.—p. 821.
Hexylcaine Hydrochloride: Preliminary Report of Its Clinical Use in Comparison with Procaine. J. E. Ruben and E. Anderson.—p. 843.
Duplication of Small Intestine. C. B. Ripstein.—p. 847.
Spinal Anesthesia Utilizing Pontocaine in Hypobaric Solution for Surgical Procedures on Anorectal Region. J. M. Duffy Jr. and D. M. Little Jr.—p. 853.
pHisoderm with Hexachlorophene (G-11): Its Integrity as Surgical Scrub. R. F. Bowers.—p. 859.
Transacromial Incision for Exposure of Shoulder Joint. H. vH. Thatcher.—p. 864.
Oxyhemography. F. W. Hartman, V. G. Behrmann and R. D. McClure. —p. 867.
Intramuscular Infusions of Protein Hydrolysate. J. J. Weinstein. —p. 870.
Etiology of Primary Varicose Veins: Histologic Study of One Hundred Saphenofemoral Junctions. F. B. Wagner Jr. and P. A. Herbut.—p. 876.
Effects of Uronic Acids, Pectins and Pectinates on Enteric Flora, Alone and in Combination with Antibiotics: I. In Vitro Studies. W. E. Wooldrige and G. W. Mast.—p. 881.
Carotid Body Tumors. H. Charache.—p. 887.
Ultraviolet Blood Irradiation Therapy (Knott Technic) in Thrombophlebitis. G. P. Miley and P. M. Dunning.—p. 892.
Six Primary Carcinomas in 1 Patient. J. Ettinger, T. B. Massell and F. B. Wilkins.—p. 894.
Carcinoma of Cecum in Young Man of Twenty-One. T. F. Keyes. —p. 898.

Meckel's Diverticulum.—Schwei and Jackson review 39 cases of Meckel's diverticulum operated on during the years 1915 to 1948. The condition occurred twice as often in males as in females. In 17 of the patients the diverticulum was without disease, in 22 it presented pathologic changes. In 11 cases the diverticulum showed inflammatory changes, 7 being acute or gangrenous. Of these, 3 diverticulums perforated and caused peritonitis. Symptoms of this type resemble those of an inflamed or perforated viscus and simulate acute appendicitis or a perforated appendix. There were 4 patients with intestinal obstruction. In 6 of the patients peptic ulceration was present in the diverticulum, and 5 of these had clinical evidence of intestinal hemorrhage. An enterogenous cyst was found in 1 patient. There were no malignant tumors in the entire group. Abdominal pain was present in all except 1 instance. Resection or excision of the diverticulum was performed in 35 of the 39 cases. All the patients recovered except the youngest and the oldest (aged 10 months and 72 years). The former had a gangrenous ileum, the latter had generalized peritonitis. A search for Meckel's diverticulum should always be made during an intra-abdominal operation, especially when the gross appearance of the organ being investigated does not fit the clinical picture.

American Practitioner, Philadelphia

4:181-242 (Dec.) 1949

Clinical Evaluation of Hypertensive Patient. M. Sokolow.—p. 184.
Production of Electrocardiographic Abnormalities by Suggestion Under Hypnosis: Case Report. L. L. Bennett and N. E. Scott.—p. 189.
Practical Considerations of Blood Volume. E. Brown and J. Hopper Jr. —p. 191.
Classification of Rheumatic Diseases with Special Emphasis on Diagnosis and Treatment of Rheumatoid Arthritis. S. R. Mettier.—p. 196.
Influence of Spleen upon the Liver. S. P. Lucia.—p. 201.
Enteric-Coated Ammonium Chloride for Control of Muscular Cramps. J. J. Sampson.—p. 205.
Diagnosis and Treatment of Viral Pneumonia. G. Meiklejohn.—p. 210.
Pneumococcic Infections in Adults at San Francisco Hospital from 1932 to 1946. J. W. Brown and J. C. Lockhart.—p. 214.
Current Therapy of Amebiasis. H. H. Anderson.—p. 218.
Laboratory Diagnosis of Amebiasis. H. G. Johnstone.—p. 222.
Proper Use of Chemotherapeutic Agents. H. Brainerd.—p. 226.
Nutritional Concepts as Revealed by Studies of Thiamine, Folic Acid and Pyridoxine Deficiency in Rhesus Monkey. J. F. Rinehart and L. D. Greenberg.—p. 230.

American Review of Tuberculosis, New York

60:683-828 (Dec.) 1949

Surgical Treatment of Recurrent and Chronic Spontaneous Pneumothorax of Nontuberculous Origin. R. H. Meade Jr. and B. B. Blades. —p. 683.
Surgical Importance of Anatomical Distribution of Pulmonary Segments. E. M. Kent.—p. 699.
*Physiological Effects of Pneumoperitoneum upon Respiratory Apparatus. G. W. Wright, R. Place and F. Princi.—p. 706.
Evaluation of Streptomycin Regimens in Treatment of Tuberculosis: Account of Study of Veterans Administration, Army, and Navy, July 1946 to April 1949. W. B. Tucker.—p. 715.
Diffuse Pulmonary Granulomatosis in Young Women Following Exposure to Beryllium Compounds in Manufacture of Radio Tubes: Report of 5 Cases. P. Slavin.—p. 755.
Tuberculosis Among Selective Service Registrants. M. Smith, L. T. Reynolds and M. E. Hand.—p. 773.
*Fatal Tension Pneumothorax Resulting from Diaphragmatic Rupture in Patient Receiving Pneumoperitoneum. S. A. Yannitelli, C. E. Woodruff, E. E. Mueller and W. L. Howard.—p. 794.

Effects of Pneumoperitoneum on Respiratory Apparatus.—The study by Wright, Place and Princi was undertaken in an effort to ascertain the quantitative aspect of variations in lung size consequent to pneumoperitoneum. Studies were made with patients in the erect and recumbent positions in 17 cases and in the recumbent position only in 2 additional cases. It was found that pneumoperitoneum causes a considerable reduction in the functional residual air, residual air and total volume of a subject in the erect position. A similar though quantitatively less decided effect is observed when the subject is studied in the recumbent position. The authors also observed the effects on the pulmonary volume and proportion of respiration performed by each lung (bronchospirometry), which were produced by adding a paralysis of the hemidiaphragm to a preexisting pneumoperitoneum. A small further reduction of functional residual air and a large reduction of complementary air, together with a reduction in function by the homolateral lung, resulted from the added paralysis. An abdominal binder caused a slight diminution of pulmonary volume in 2 patients and a considerable diminution in a third when applied in the presence of pneumoperitoneum. The maximum breathing capacity was only slightly reduced by the induction of pneumoperitoneum. The authors believe that pneumoperitoneum, if fully established, is an effective method of reducing the size or state of distention of the lung. It is more adequate in this respect than paralysis of the hemidiaphragm. Since the modern concept of the degree of collapse desired in intrapleural pneumothorax commonly makes use of less than a 50 per cent collapse of the lung, pneumoperitoneum plus recumbency is as effective in collapsing the lung as is pneumothorax, unless virtually complete collapse of the lung is desired.

Fatal Pneumothorax Resulting from Diaphragmatic Rupture During Pneumoperitoneum.—Yannitelli and his associates report that the induction of pneumoperitoneum in a girl aged 16 resulted in an elevation of the left hemidiaphragm a maximum of two and one-half interspaces and the right hemidiaphragm two interspaces. Pneumoperitoneum refills of 1,000 to 1,500 cc. of air were continued at weekly or ten day intervals, maintaining the diaphragms at the aforementioned levels. After some months of this treatment, and twenty days after the last refill, the patient noted sudden onset of mild subscapular pain aggravated by deep respiration. She was given sedatives. Roentgenographic examination revealed partial collapse of the right lung, with a small amount of fluid at the base. There was displacement of the heart and trachea to the left. The roentgenogram revealed two adjacent, bleblike shadows, each 7 mm. in diameter, projecting above the middle of the right leaf of the diaphragm. Later pneumoperitoneum refills were cautiously resumed and continued for several months. On Sept. 8, 1948 the patient received her usual refill of 1,300 cc. of air with initial pressures of plus 3, plus 5 and final pressures of plus 6, plus 8. Both diaphragms were well elevated. During the day of September 16 the patient was exceptionally boisterous, laughing and moving about in bed considerably. At 9:30 that evening she became somewhat apprehensive and complained of right shoulder pain, for which she was given sedatives. At midnight

the patient appeared normal except for nervousness and mild pain. Additional sedatives were given. At 3:10 a. m. her respirations seemed more labored, and she was found dead at 3:50 a. m. A postmortem interpretation of the cause of death was tension pneumothorax and right-sided myocardial dilatation following rupture of the diaphragm. The authors point out that the patient's diaphragm was maintained at a fairly high level for ten months before her first episode of rupture. During this period the muscle fibers were apparently stretched apart sufficiently to permit a small rupture through the diaphragm, resulting in the formation of a bleb on its pleural surfaces. Two other factors might possibly have played a role in precipitating the rupture of the bleb at such long intervals after the previous refills. As the diaphragm descended, the relation of the bleb to the base of the right lung changed. This may have been sufficient to break a seal that had been established between these two structures. Second, it appears that the coughing, laughing and boisterousness of the patient the evening before she died was an important factor in initiating the terminal episode of rupture. It is probable that the bleb was ruptured by the pull or tear of already stretched adhesions during this excessive activity of the diaphragm.

Annals of Allergy, Minneapolis

7:585-726 (Sept.-Oct.) 1949. **Partial Index**

Mold Fungi in Etiology of Respiratory Allergic Diseases. L. O. Dutton.—p. 585.
Procedure for Determination of Aerosol Delivery and Stability During Nebulization. H. A. Abramson, B. Sklarofsky and C. Reiter.—p. 612.
Penicillin Sensitivity. F. K. Hansel.—p. 619.
Inhalant Allergy. H. J. Rinkel.—p. 625.
Topical Application of Thephorin: Study of Frequency of Eczematous Sensitization. C. W. Laymon, J. F. Madden and F. J. Schmid. —p. 646.
Corn Sugar as Allergen. T. G. Randolph and L. B. Yeager.—p. 651.
Use of Bacitracin, New Antibiotic, in Aerosol Form: Preliminary Observations. S. J. Prigal and M. L. Furman.—p. 662.
Diatrin Hydrochloride: New Antihistaminic Agent for Treatment of Pruritis and Allergic Dermatoses. F. C. Combes, R. Zuckerman and O. Canizares.—p. 676.
Possible Uses of Delayed-Action Antihistaminic: Clinical Trials. M. M. Hartman.—p. 679.

Endocrinology, Springfield, Ill.

45:451-548 (Nov.) 1949. **Partial Index**

Bioassay of Hypophyseal Growth Hormone: Tibia Test. F. S. Greenspan, Choh Hao Li, M. E. Simpson and H. M. Evans.—p. 455.
Changes Induced in Iodine Metabolism of Rat by Internal Radiation of Its Thyroid With I^{131}. D. D. Feller, I. L. Chaikoff, A. Taurog, H. B. Jones.—p. 464.
Effect of Growth Hormone on Hepatic and Renal Acid and Alkaline Phosphatases. J. C. Mathies, O. H. Gaebler and L. Palm.—p. 480.
Oxygen Consumption and Plasma Protein-Bound Iodine Following Elemental Iodine Injections. S. B. Barker and H. J. Lipner.—p. 485.
Temporary Nature of Inhibitory Action of Excess Iodide on Organic Iodine Synthesis in Normal Thyroid. J. Wolff, I. L. Chaikoff, R. C. Goldberg and J. R. Meier.—p. 504.
Relationship of Mouse Adrenal Cortex to Pituitary. I. C. Jones. —p. 514.

Gastroenterology, Baltimore

13:391-492 (Nov.) 1949

*Liver Function in Chronic Alcoholic Patients: II. Correlation Between Elements of History and Presence of Liver Dysfunction as Indicated by Laboratory Tests. W. L. Voegtlin, W. R. Broz, W. E. Rupper and M. M. Robinson.—p. 391.
*Experimental Observations on Cardiospasm in Man. S. Wolf and T. P. Almy.—p. 401.
Simple Explanation for Cardiospasm and Hirschsprung's Disease. W. C. Alvarez.—p. 422.
Multiple Polyposis of Colon. G. H. Schantz.—p. 430.
Increased Activity of Intestines Following Injection of Epinephrine. N. B. Dreyer and H. I. Zauder.—p. 440.
Effect of Dibutoline on Motility of Stomach and Small Intestine in Man—X-Ray Study. F. C. Bone, M. B. Crow, D. P. White and J. M. Ruffin.—p. 443.

Liver Function in Chronic Alcoholic Patients.—The patients comprising this series studied by Voegtlin and his associates were treated at a private hospital for alcoholism. Most studies on the relation of alcohol to portal cirrhosis have been done on patients with cirrhosis by determining how many were also alcoholic addicts. This investigation is different in that the authors have selected known alcoholic addicts and have attempted to determine the incidence of portal cirrhosis among them. An attempt was made to select certain factors in the history and symptomatology of alcoholic patients which might be of value in predicting the likelihood of hepatic dysfunction being present in any given case. In this the study has been a failure, because the absence of clearcut trends and the paucity of significant statistical differences indicate that not a single factor which the authors considered was of great importance in this respect. The study has shown that there is no tendency toward the presence of more serious or frequent hepatic dysfunction in those patients in the older age groups or with the longer drinking history. This is taken as evidence that alcoholism does not predispose to the development of any progressive degenerative disease of the liver such as portal cirrhosis. The slight tendency for less frequent and severe hepatic dysfunction to be present in periodical alcoholic addicts, as compared to steady drinkers, suggests that the characteristic type of hepatic dysfunction seen in chronic alcoholism is reversible and susceptible to improvement during the abstinent phases of the periodical alcoholic addict. This again suggests that the process is not portal cirrhosis. Certain symptoms seen in chronic alcoholic patients such as changes in tolerance or response to alcohol, delirium tremens or sexual impotence appear to be independent of the presence or absence of hepatic dysfunction. The study indicates that ingestion of alcohol, even in excessive amounts, before, during and after an episode of acute hepatitis does not necessarily predispose the liver to serious or irreversible damage.

Experimental Observations on Cardiospasm.—Wolf and Almy made repeated fluoroscopic observations of swallowed barium sulfate in 14 patients with well established cardiospasm. They found that the esophageal obstruction of cardiospasm was often associated with decided hypermotility of the lower two thirds of the esophagus. Irregular contractile activity was noted even in the presence of moderate dilatation of the organ. Only when the esophagus was widely dilated and greatly elongated was the motility absent. The degree of esophageal obstruction in 9 of 14 subjects with cardiospasm could also be intensified by increase in the contractile state of the diaphragm, as in a deep breathing. Exacerbations or remission of symptoms in these subjects could be correlated with periods in their lives of stress or relative security. In short term experimental observations it was noted that a discussion of emotionally charged topics was associated with hypermotility and obstruction in the esophagus, while relative security and relaxation were associated with diminution or disappearance of the phenomena of cardiospasm. Esophageal changes of cardiospasm in a normal subject, were induced by application of local noxious stimuli in the form of heat, cold and a chemical irritant. A few among other normal subjects reacted with cardiospasm to general threats and stresses, including symbolic ones. These data suggest that cardiospasm may occur as part of a biologic reaction to stress, functional and reversible in its early stages.

Georgia Medical Association Journal, Atlanta

38:477-524 (Nov.) 1949

Dihydrostreptomycin: Its Use in Urologic Problems in General Practice. J. H. Semans.—p. 477.
Neoplastic Disease of Ureter. W. L. Champion, M. F. Fowler, R. C. Coleman Jr. and T. J. Florence.—p. 481.
Exstrophy of Urinary Bladder: Surgical Treatment. M. K. Bailey, C. A. Fort and H. C. Harlin.—p. 484.
Conservatism in Prostatic Surgery. R. Bell and R. F. Stinson.—p. 488.
Present-Day Management of Prostatic Obstruction. C. L. Prince. —p. 490.
Retropubic Prostatectomy. W. H. Bennett and J. D. Moffett.—p. 494.
Adrenal Surgery. D. E. Beard and W. E. Goodyear.—p. 500.
Appendices Epiploicae as Cause of Acute Abdominal Pain. R. E. Campbell and J. Canipelli.—p. 503.

Iowa State Medical Society Journal, Des Moines

39:545-594 (Dec.) 1949

Indications for Cesarean Section. W. A. Boice.—p. 545.
Surgical Treatment of Varicose Veins. J. W. Dulin.—p. 551.
Angiocardiography. P. G. Keil, C. A. Voelker and D. J. Schissel.—p. 553.
Medical Treatment of Thyrotoxicosis. H. M. Hurevitz.—p. 556.
Evaluation of Diagnosis and Treatment of External Otitis. C. M. Kos. —p. 560.

Journal of Bacteriology, Baltimore

58:717-834 (Dec.) 1949. **Partial Index**

Staphylococcal Hyaluronidase. M. M. Davison, M. A. Derow and B. S. Walker.—p. 717.
Determination of Lysozyme. A. N. Smolelis and S. E. Hartsell.—p. 731.
Action of Streptomycin. E. L. Oginsky, P. H. Smith and W. W. Umbreit.—p. 747.
Stimulation of Growth of Strain of Corynebacterium Diphtheriae by Polyvinyl Alcohol. S. Cohen.—p. 783.
Characterization of Agglutinating Principle in Chorioallantoic Fluid Responsible for Clumping of Certain Strains of Staphylococcus Aureus. E. W. Shrigley and E. S. Maculla.—p. 791.
Inhibition of Bacterial Esterases by Chloramphenicol (Chloromycetin). G. N. Smith, C. S. Worrel and A. L. Swanson.—p. 803.
Cobalt and Bacterial Growth, with Special Reference to Proteus Vulgaris. A. L. Schade.—p. 811.

Journal of Investigative Dermatology, Baltimore

13:309-378 (Dec.) 1949

McClure-Aldrich Test in Dermatology with Special Reference to Bullous Dermatoses. O. Canizares, F. C. Combes, S. Simuangco and J. Kaufman.—p. 325.
Squalene in Sebum and Sebum-Like Materials. H. Sobel.—p. 333.
Trichophyton Mentagrophytes (Variety Nodular): Mutant with Brilliant Orange-Red Pigment Isolated in 9 Cases of Ringworm of Skin and Nails. L. K. Georg and E. H. Maechling.—p. 339.
Investigation of Contact-Type Dermatitis Due to Compound Tincture of Benzoin. K. Steiner and W. Leifer.—p. 351.
Hypospray and Its Relation to Dermatology: Preliminary Report. L. E. Larrick and R. G. Thompson.—p. 361.

Journal of Lab. and Clinical Medicine, St. Louis

34:1623-1806 (Dec.) 1949. **Partial Index**

Amino Acid Excretion in Degenerative Diseases of Nervous System. H. Porter.—p. 1623.
*Parenteral Nutrition: X. Observations on Use of Fat Emulsion for Intravenous Nutrition in Man. S. W. Gorens, R. P. Geyer, L. W. Matthews and F. J. Stare.—p. 1627.
*Absorption and Disposition of Orally Administered I^{131}-Labeled Neutral Fat in Man. M. M. Stanley and S. J. Thannhauser.—p. 1634.
Effect of Splenectomy on Toxicity of SR^{89} to Hematopoietic System of Mice. L. O. Jacobson, E. L. Simmons and M. H. Block.—p. 1640.
Japanese B Encephalitis: Report of Five Cases. N. F. Wyatt.—p. 1656.
Pancreatitis in Infectious Mononucleosis. J. Myhre and S. Nesbitt.—p. 1671.
Case of Congenital Idiopathic Methemoglobinemia. B. Fisher and J. W. Price.—p. 1676.

Fat Emulsion in Parenteral Nutrition.—Gorens and co-workers administered intravenously a fat emulsion consisting of 15 per cent coconut oil, 4.3 per cent dextrose and a combination of 0.5 per cent soybean phosphatides and 1 per cent polyglycerol esters as stabilizers to 11 patients with a variety of common ailments. These ailments resulted in weight loss of such an extent that provision for adequate calories was imperative. Eight of these patients were between the ages 24 and 73, 2 were 4 and 6½ years and 1 was 7 weeks old. The emulsion furnished 1,600 calories per liter and was given at rates ordinarily used for administering dextrose or saline solutions. Daily amounts up to 3 Gm. fat per kilogram of body weight were given to adults and 6 Gm. fat per kilogram of body weight to the infant. Infusion periods ranged from three to twenty-seven consecutive days. The emulsion was effective as indicated by favorable clinical response, the prevention of weight loss and the maintenance of positive nitrogen and potassium balance. Three patients died, 1 approximately one month after the last fat infusion, 1 three months after the last infusion and the third eighteen hours after the last infusion of fat. Autopsy of 2 patients showed that the fat emulsion had not produced any pathologic change, either gross or microscopic. An increase in temperature in 3 patients was observed regularly following a single administration of a certain amount of fat. These temperature rises were probably due to pyrogenic materials in the fat and not to the fat per se.

Absorption and Disposition of Oral I^{131}-Labeled Fat in Man.—Stanley and Thannhauser studied the absorption and utilization of fat in 10 normal persons and in 7 patients, 2 of them with "idiopathic" hyperlipemia and 1 with a nephrotic syndrome. Characteristic curves of absorption and utilization of physiologic amounts of fat taken by mouth were demonstrated by the use of unsaturated fats iodinated with iodine 131. The proportion of the administered radioactive iodine which was collected by the thyroid and excreted in the urine, as well as the magnitude of the water-soluble portion in the serum, indicated the extent of breakdown of the labeled fat. Breakdown of 50 to 73 per cent of the orally administered iodinated fat took place under these conditions in the normal persons within twenty-four hours. Patients with "idiopathic" hyperlipemia and the nephrotic syndrome utilized the labeled fat much more slowly.

Journal of Nervous and Mental Disease, New York

110:464-588 (Dec.) 1949

*Topectomy: Surgical Technique, Psychiatric Indications and Postoperative Management. J. L. Pool, R. G. Heath and J. J. Weber.—p. 464.
Organic Paranoid Syndrome. G. N. Thompson and J. M. Nielsen.—p. 478.
Intravenous Alcohol and Early Convulsive Shock in Treatment of Exhaustion Due to Mental Disorder. H. A. Perry and S. Levy.—p. 497.
Entropy Changes in Mental Activity. M. Ostow.—p. 502.
Effect of Insulin Shock Therapy on Glucose Metabolism in Schizophrenia. H. F. Borenz, D. B. Schuster and G. J. Downey.—p. 507.
Mental Hygiene Clinic: Its Organization and Operation. M. H. Adler, A. F. Valenstein and J. J. Michaels.—p. 518.

Topectomy.—Pool and his associates removed a limited amount of cortex bilaterally from the region of Brodmann's area 9. Since this did not always seem a sufficient amount and since the caudal part of area 9 lay so close to the motor cortex, cortical removals were later confined to the rostromedial aspect of each frontal lobe so as to include portions of areas 9 and 10. Medially, all such removals were carried down to the region of the upper or the dorsal margin of the cingulate gyri to the level of the inferior longitudinal sinus. While in some cases part of the cingulate gyri and/or the frontal poles were also removed, there seemed to be little difference in the postoperative behavior in these cases and in those in which these regions had not been ablated. Hence, in the topectomy currently practiced, cortical removal has been limited to the rostromedial portions of what is believed to represent Brodmann's areas 9 and 10. A further modification of technic was evolved, consisting of ligation of the major nutrient arteries to the area of the cortex. The authors describe the preoperative treatment and the technic of the operation on the basis of a total of more than 95 topectomy operations. There has been no operative fatality, and the usual postoperative course of the patient subjected to topectomy differed considerably from that of the patient who had undergone a standard prefrontal lobotomy. The patient subjected to topectomy tended to be less depressed and disoriented, especially during the first twenty-four hours after operation. However, from the second to the fifth postoperative day, and sometimes longer, the patient often displayed hostility and resentment, but these subsided so that the patient could be discharged on the tenth to fourteenth day. Postoperative hemorrhage occurred in 2 cases and was successfully treated by reelevation of the operative flap and evacuation of the hematoma. Temporary urinary incontinence occurred in one third of the cases, lasting an average of ten days. Retention of urine occurred in 3 cases but was not permanent. In 1 patient transitory diffuse peripheral neuritis developed. The seizure incidence was 10 per cent. Operation is followed by an alteration of affective or emotional responses. Rage, joy and fear may still be felt, the change being that the patients do not have the same subjective intensity as they had before operation. The poorer results and failures occur most often among schizophrenic patients. The few neurotic patients, mostly those with compulsive obsession, who were subjected to topectomy responded well. Topectomy, by removal of the painful emotion in depressed patients, permits resumption of the premorbid existence. Frontal lobe operation attacks an important aspect of the illness and greatly aids the psychiatric treatment, but without adequate psychiatric treatment the remission rate falls considerably.

Maine Medical Association Journal, Portland

40:345-386 (Dec.) 1949

Organization and Administration of Emergency Polio Service. F. C. Curran.—p. 345.
Coordination-Cooperation vs. Polio. C. W. Ruhlin.—p. 347.
Clinico-Pathological Exercise: Case Presented at Eastern Maine General Hospital, Bangor, Maine. R. C. Wadsworth.—p. 352.
Clinical Evaluation of Newer Anti-Histaminic Chlor-Trimeton. M. A. Vickers and R. J. Barrett.—p. 356.
Cervicitis. D. Coulton.—p. 358.
Cysts and Sinuses of Neck. E. A. Gaston and W. A. Albro.—p. 361.
Carcinoma of Colon. A. C. Todd.—p. 365.
Meconium Ileus of Newborn: Case Report. H. F. Rheinlander.—p. 368.

Medical Annals of District of Columbia, Washington

18:619-680 (Dec.) 1949

Acute Pancreatitis: Review of Present Concepts as Related to 46 Cases in District of Columbia. J. Selby.—p. 619.
Brief Review of Use of Adrenal Cortical Steroids and Related Substances in Treatment of Rheumatic Fever and Rheumatoid Arthritis. R. Liefmann and M. P. Schultz.—p. 629.
Complications of Measles in Childhood: Review of 60 Cases. J. M. Lo Presti, H. Ahari and W. F. Burdick.—p. 633.
Simple Method for Management of Scalp Wounds. I. P. Frohman.—p. 639.
Histoplasmosis of Larynx: Report of Case. M. Parke and S. Burtoff.—p. 641.

New England Journal of Medicine, Boston

241:951-992 (Dec. 15) 1949

Value of Thoracoabdominal Incision in Removal of Kidney Tumors. R. Chute, L. Soutter and W. S. Kerr Jr.—p. 951.
*Syphilis in Pregnancy: Clinical Study of Factors Responsible for Congenital Syphilis. A. Heyman and J. R. McCain.—p. 960.
Thrombasthenia and Thrombocytopenic Purpura: Report of Case Demonstrating Qualitative and Quantitative Inadequacy of Platelets. B. Alexander and G. Landwehr.—p. 965.
Acribia. H. J. L. Marriott.—p. 968.
Vitamin Supplementation in Health and Disease. P. J. Culver.—p. 970.
Generalized Arteriosclerosis with Ruptured Arteriosclerotic Aneurysm of Abdominal Aorta.—p. 978.
Choledocholithiasis. Fistula, Cystic Duct to Duodenum. Obstructive Biliary Cirrhosis. Splenomegaly. Cardiac Hypertrophy.—p. 981.

Congenital Syphilis.—According to Heyman and McCain cases of infantile congenital syphilis continue to appear in significant numbers. They investigated the records of 77 women who delivered syphilitic infants at Grady Memorial Hospital in Atlanta, Ga., during the last four years. Approximately a fourth of these women had negative serologic reactions for syphilis in pregnancy and had not received prenatal treatment for syphilis. The majority of these patients are believed to have been in the incubation period of the disease at the time of the negative reaction or to have acquired an initial or recurrent syphilitic infection later in pregnancy. The authors emphasize the importance of repeating serologic tests near term to detect syphilis acquired late in pregnancy. The maternal infection almost always had existed less than five years prior to birth of the syphilitic infant. An occasional patient transmitted syphilis to her child even though she had had the disease for as long as eleven years. Half the women who were given prenatal treatment had received 11 to 20 injections of arsenoxide during pregnancy. The authors stress the inadequacy of arsenical therapy late in pregnancy. Penicillin therapy is believed to be the treatment of choice in prenatal syphilis. Women should be urged to seek prenatal care early in pregnancy.

New Jersey Medical Society Journal, Trenton

46:547-596 (Dec.) 1949

Needle Biopsy of Liver: Critical Evaluation. T. J. White, C. M. Leevy, N. F. Kemp and others—p. 549.
Regional Anesthesia for Upper Abdominal Surgery. N. B. Kornfield.—p. 556.
*Proctosigmoidoscopic Examinations in General Practice. L. M. Townsend.—p. 558.
Calcification of Annulus Fibrosus. S. F. Alexander and S. Alexander.—p. 562.
Pulmonary Heart Disease. P. K. Bornstein.—p. 565.
Multiple Positive Patch Test Reactions. S. L. Hanfling.—p. 568.
Ringworm of Scalp. M. H. Holland.—p. 570.
Selection of Blood Donors. T. K. Rathmell and E. L. Bowser.—p. 571.

Proctosigmoidoscopic Examinations in General Practice.—Townsend discusses routine proctosigmoidoscopic examinations in a general medical practice. By far the greatest majority of patients so examined had no complaints suggestive of anorectal or colonic disease. The examinations were made for the purpose of discovering asymptomatic sigmoid or rectal cancers or polyps. Of the 300 patients so examined only 25 were referred by other physicians. In these 25 patients the incidence of serious pathologic conditions was disproportionately high. The total group probably presents a fair cross section of patients seen by a family physician. These patients were not all prepared for examination by catharsis or enemas. The knee-shoulder position was used. The aim was to determine the amount and type of pathologic lesions that may be detected without special preparation of the patient. Two hundred and eighty-five examinations were considered complete. Seven patients were found with malignant or premalignant lesions; a short history of each case is given.

North Carolina Medical Journal, Winston-Salem

10:625-682 (Dec.) 1949

SYMPOSIUM ON TOXEMIA OF PREGNANCY

Prenatal Care in Rural Area. F. Fuller.—p. 625.
Management of Hypertensive Cardiovascular and Renal Disease in Pregnancy. M. I. Griffith.—p. 627.
Management of Eclampsia. J. C. Burwell Jr.—p. 630.
Drug Therapy for Asthmatic Children. S. C. Dees.—p. 634.
Management of Vomiting in Acute Infections Without Use of Parenteral Fluids. A. H. Pate.—p. 638.
Diagnosis and Management of Jaundice in General Practice. W. H. Flythe.—p. 640.
Tests for Urinary Sodium Chloride. W. B. Burwell.—p. 645.
Improved Instruments for Diagnosis of Pelvic Lesions by Hysterogram and Water Hysteroscope. W. B. Norment.—p. 646.
Blastomycosis Complicating Boeck's Sarcoid: Report of Case. J. S. Hiatt Jr. and T. N. Lide.—p. 650.

Plastic and Reconstructive Surgery, Baltimore

4:489-582 (Nov.) 1949

Repair of Bilateral Cleft Lip. W. C. Huffman and D. M. Lierle.—p. 489.
*Successful Homotransplantation of Skin from Parents to Son. J. E. Kearns Jr. and S. E. Reid.—p. 502.
Complete Avulsion of Skin of Penis and Scrotum; Surgical, Endocrinological and Psychological Treatment. H. Baxter, M. Hoffman, E. Smith and K. Stern.—p. 508.
Nasopharyngeal Stenosis: Correction by Transposed Flaps. H. S. Vaughan.—p. 522.
Cancer of Face: Treatment and Plastic Repair. G. B. New.—p. 528.
Use of Removable Acrylic Prosthesis to Retain Mandibular Fragments and Adjacent Soft Tissues in Normal Position After Surgical Resection. G. E. Ward, R. S. Williamson Jr. and J. O. Robben.—p. 537.
Utilization of Tube Pedicle in Reconstruction of Facial Defects. C. F. Steiss.—p. 545.
Use of Dorsal Skin Flap for Coverage of Palmar Defects After Aponeurectomy for Dupuytren's Contracture. J. M. Bruner.—p. 559.

Successful Transplantation of Skin from Parents to Son.—Kearns and Reid present the case of a boy, aged 9, who had extensive, chronically infected burns which had been unsuccessfully treated with autografts. Split thickness skin grafts were transferred from each parent to the boy. Even though two grafts were successfully applied from each donor, there was no evidence of anaphylactoid response. Anemia and hypoproteinemia were treated before operation. Chronic infection was combated by local application of antibiotics. Thorough and deep débridement of the recipient site was achieved by local application of 80 per cent silver nitrate at operation, followed by excision or curettage of the eschar thus formed down to the uninfected layers below. Grafts were prepared by saturation with plasma and applied after application of thombin solution to the débrided recipient sites.

Psychosomatic Medicine, New York

11:187-248 (July-Aug.) 1949

Psychiatric Aspects of Vagotomy: II. Psychiatric Study of Vagotomized Ulcer Patients with Comments on Prognosis. T. S. Szasz.—p. 187.
Physiologic and Psychologic Interrelationships in Diabetes in Children. H. Bruch.—p. 200.
Emotional Factors in Precipitation of Recurrent Diabetic Acidosis. H. Rosen and T. Lidz.—p. 211.
Anthropology and Psychosomatics. J. Henry—p. 216.
Life Situations, Emotions, and Bronchial Mucus. I. P. Stevenson and H. G. Wolff.—p. 223.
Motor Attitudes and Psychotherapy. E. Ascher.—p. 228.
The Infant in the Adult: Induced Regression in Therapy of Psychogenic Gastrointestinal Disorder: Case Report. L. T. Maholick.—p. 235.

South Carolina Medical Assn. Journal, Florence

45:359-394 (Dec.) 1949

Echinococcus Infection: Report of Case in Immigrant in South Carolina. W. C. Hollifield and R. Wilson Jr.—p. 359.
Recent Advances in Diagnosis and Treatment of Rheumatic Fever. W. Weston Jr.—p. 362.
Prolapse of Meckel's Diverticulum with Intussusception: Report of Case. A. J. Katzberg.—p. 366.
Public Health Problems of Hookworm Disease in South Carolina. J. H. Arnold.—p. 367.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:1307-1366 (Dec. 10) 1949

Can a Scientific Society Be Stable? B. Russell.—p. 1307.
Visceral Actinomycosis. V. Z. Cope.—p. 1311.
*Vagotomy for Peptic Ulcer: Indications and Results. I. M. Orr and H. D. Johnson.—p. 1316.
Use of Procaine Penicillin with Aluminium Monostearate in Adults. E. J. Wanbe, J. Colquhoun and J. Burke.—1319.
*Herpes Zoster After Irradiation. F. Ellis and B. A. Stoll.—p. 1323.
Male Subfertility: Interim Report of 3,182 Cases. H. A. Davidson. —p. 1328.
Thumb Reconstruction by Transfer of Big Toe. P. Clarkson and R. Furlong.—p. 1332.

Vagotomy for Peptic Ulcer.—Orr and Johnson present observations on 215 patients subjected to vagotomy over the last five years. The percentage of failures among the early cases was high, but as the technic improved the proportion of incomplete vagotomies decreased, as did the proportion of failures. During the second and third years close follow-ups revealed the limitations of vagus resection in the treatment of duodenal ulcer, and some of the complications of vagotomy were recognized. The observations made in this second period showed that complete vagotomy resulted in a considerable fall in free acid and that the low acid level was maintained; but it also showed that in spite of the fall in free acid level, 25 per cent of the patients continued to complain of ulcer symptoms or had a recurrence after an initial period of well-being. Furthermore, while 75 per cent of the patients who had undergone vagotomy remained free from ulcer symptoms, certain unpleasant side effects appeared. During the third and fourth years of study an analysis of results suggested that some of those who had been subjected to vagotomy were unsuitable subjects and that others presented too complicated a picture to be dealt with adequately by vagotomy alone, and combined operations were undertaken, such as vagotomy plus gastric resection or gastroenterostomy. The remaining period has confirmed that early uncomplicated cases of duodenal ulcer associated with high interdigestive secretion of free acid may obtain lasting benefit from vagotomy alone. For patients with a history of hemorrhage, perforation, scarring or deep crater formation, more radical operations are indicated. The results of the combined operations have been gratifying.

Herpes Zoster After Irradiation.—Ellis and Stoll review observations on 45 patients in all of whom herpes zoster developed after irradiation. Thirty-nine of these had malignant disease (including 24 with carcinoma of the breast), and 6 had nonmalignant disease. The analysis of these cases shows maximal incidence of zoster at the level of the neoplasm, and thus of the site of irradiation; involvement by the zoster of either the same or, to a lesser extent, the side of the body opposite to that irradiated; a maximal incidence of zoster between three and six months following the treatment, with a gradually diminishing incidence up to two years. The authors believe that the time relationship between the development of the zoster and the previous irradiation provides strong evidence that irradiation is implicated as a causative factor in zoster. Late irradiation reactions in all parts of the body associated with the relative ischemia and fibrosis which follow endothelial proliferation usually tend to develop at an interval of three to six months after treatment. A delayed vascular deficiency and gliosis in the spinal root ganglion or delayed fibrosis in the skin with involvement of the nerve endings might cause activation of a latent zoster virus. Regarding the question as to how the irradiation may be concerned in the etiology of herpes, the authors mention that the skin area (and thus the cutaneous nerves also) corresponding to the level involved by zoster later had in the majority of cases been irradiated. It is suggested that zoster may result either from a systemic mechanism following the release of substances set free by irradiation, or possibly from an effect on the cord through the afferent nerves of the irradiated area. Herpes zoster is relatively rare after roentgen treatment; even in a large group of cases of carcinoma of the breast treated postoperatively with roentgen rays the number developing zoster is small. Immunity conferred by a previous attack of zoster or varicella may partly explain this. Previous attempts to correlate zoster with cancer or reticulosis have been based on the hypothesis that the zoster was due to infiltration by the underlying disease of the spinal ganglions or other parts of the afferent nervous reflex arc. No other authors seem to have correlated the incidence of zoster with the administration of roentgen rays in cases when such infiltration was absent.

Irish Journal of Medical Science, Dublin

287:787-834 (Nov.) 1949

Biological Interlinkage of Acid-Alkali Formation with Ion Transport and Synthetic Reduction. E. J. Conway.—p. 787.
Redox Theory of Hydrochloric Acid Production by Gastric Mucosa. E. J. Conway.—p. 801.
Choice of Anaesthetic for Caesarean Section. R. W. Shaw.—p. 805.
Spontaneous Haematoma of Rectus Abdominis Muscle. F. J. Morrin.—p. 815.
Effect of Blood Glucose Concentration on Alkaline Haematin Method of Haemoglobin Estimation. J. D. Kennedy and T. Rea.—p. 821.
Calcification of Placenta. E. Solomons.—p. 823.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

56:741-948 (Oct.) 1949. **Partial Index**

*Rh Immunization in Pregnancy. J. Murray and M. Taylor.—p. 741.
Stromatous Endometriosis: Report of 5 Cases. W. W. Park.—p. 755.
*Nature of Stromatous Endometriosis. W. W. Park.—p. 759.
Convulsive Seizures, Questionably Eclamptic, Diagnosed Solely by Placental Examination (Case Report). S. R. Poliakoff and R. A. Bartholomew.—p. 777.
Bipartite Placenta with Report of Case. W. H. Carlisle.—p. 779.
Primary Uterine Inertia. D. J. MacRae.—p. 785.
Repair of Placental Site in Rabbit. M. M. Bull.—p. 799.
Report on Series of 129 Cases of Cancer of Corpus Uteri. G. Dearnley.—p. 819.
Oxytocic Drugs in Third Stage of Labour. D. A. F. Shaw.—p. 833.
Treatment of Contraction Ring Dystocia. W. G. Mills.—p. 838.
Essay on Physiology of Third Stage of Labour. J. R. C. Burton-Brown.—p. 847.
Factors Determining the Size of the Newborn. H. H. Knaus.—p. 856.
Myasthenia Gravis Complicating Pregnancy. A. Gunn and B. W. Sanderson.—p. 868.

Rh Immunization in Pregnancy.—Murray and Taylor believe that it should be increasingly possible to make a provisional prognosis and plan of management of cases during pregnancy instead of awaiting the birth of the baby. They report observations on 64 cases of isoimmunization. All patients attending the hospital's antenatal department had blood withdrawn on their first visit for Wassermann and Rh testing. The serum of those found to be Rh negative was tested for antibodies. The blood of the husband of every Rh-negative woman was tested for the presence of antigen D, but only when the mother had an antibody in her serum was the husband's blood genotyped. Cord blood of the infants of all Rh-negative women was tested for sensitization of cells and the presence of antigen D. In cases in which an antibody had been found during pregnancy, hemoglobin estimations, red cell, nucleated cell and differential counts were also done on capillary blood taken from the babies immediately after birth. The presence of an antibody throughout pregnancy was as indicative of an unfavorable prognosis as a previous history of hemolytic disease. It was concluded that the findings of an antibody within the first four months of pregnancy indicates previous immunization. Antibodies should be tested for between 8 and 12 weeks, at 30 weeks and at 36 weeks. Labor should be induced at about 36 weeks when antibodies are present. Exchange transfusion of the Rh-positive baby should be undertaken when anemia is present, when there is a previous history of affected babies or when an antibody has been present for more than four weeks.

Stromatous Endometriosis.—Park believes that the published accounts of so-called stromatous endometriosis of the uterus demonstrate that its macroscopic and microscopic features are distinctive enough for it to be accepted as a pathologic entity. The cases so far reported total about 50. Park discusses the aspects of this condition, which occurs most frequently during the second half of the reproductive period. Examination of microscopic sections has led to the conclusion that the lesion is not necessarily derived from the endometrial stroma but that it may arise at one or many points within the wall of the uterus. It was assumed that adenomyosis may also

be a tissue malformation of in situ development. Adenomyosis, "stromatous endometriosis," carcinosarcoma of the uterus, the mixed mesodermal tumors and some other unusual tumors of the uterus may be grouped together as conditions which cannot be fitted satisfactorily into current classifications of uterine pathology. The suggestion has been made that they are related maldevelopments of tissue. The author feels that there is no need to define stromatous endometriosis as either malignant or nonmalignant. Similarly a rigid name for the neoplasm is not essential. "Stromatous endometriosis" is so misleading that it might well be dropped. "Stromatoid new growth of the uterine wall" is perhaps the best term, but it is cumbersome. "Stromatoid mural sarcoma" might be more convenient. In 5 of the 43 cases reviewed the patient died as the direct result of recurrence and local spread of the neoplasm.

Journal of Tropical Medicine and Hygiene, London

52:243-264 (Dec.) 1949

Splenectomy in Treatment of Kala-Azar. L. E. Napier.—p. 243.
Tropical Phlebitis and Its Relation to Myositis Tropica. M. Gelfand. —p. 248.
Tuberculous Lymphadenitis in Nigerian Children. D. B. Jelliffe. —p. 251.

Lancet, London

2:1067-1114 (Dec. 10) 1949

Survey of Physical Fitness in Ceylon. H. Cullumbine.—p. 1067.
*Influence of Heart-Rate on Cardiac Output: Studies with Digoxin and Atropine. H. G. Kelly and R. I. S. Bayliss.—p. 1071.
*Source of 2 Hospital-Infected Cases of Tetanus. S. Sevitt.—p. 1075.
Non-Traumatic Thrombosis of Carotid Artery. N. O. Ameli and D. W. Ashby.—p. 1078.
*Seasonal Variations in Thyrotoxicosis. M. E. Morgans and W. R. Trotter.—p. 1083.
*Electric-Blanket Treatment of Rheumatoid Arthritis. E. Frankel. —p. 1084.
Q Fever: Report of Case. W. G. Manderson.—p. 1085.

Heart Rate and Cardiac Output: Effect of Digoxin and Atropine.—Kelly and Bayliss found that when digoxin is given in cardiac failure the rise in cardiac output is as pronounced in patients with sinus rhythm as in those with auricular fibrillation. There is no relation between the degree of slowing and the increase in cardiac output. Relief of venous congestion is also independent of the degree of slowing. Improvement in cardiac output is equally probable whether the initial ventricular rate is slow or fast. In normal hearts atropine acceleration is accompanied with a fall in right auricular pressure and a rise in cardiac output. Patients with heart disease showed essentially similar responses. There was no evidence that acceleration so induced either depressed cardiac output or increased venous congestion. Given after digoxin in fibrillating hearts, atropine can reverse the slowing effect without counteracting either the rise in cardiac output or the fall in venous pressure caused by digoxin. Similarly in patients with sinus rhythm atropine acceleration has no adverse effect on cardiac output or venous pressure after digitalization. The presence or absence of cardiac slowing plays no measurable part in producing the immediate hemodynamic improvements following digitalization.

Hospital-Infected Cases of Tetanus.—Sevitt cites histories of 2 patients who had tetanus after surgical treatment in the same hospital. One patient died; the other recovered. Discussing the probable source of these tetanus infections, the author says that building repairs were being done on part of the operating room suite and here animal hair was being mixed with plaster powder. The hair gave a heavy growth of various strains of anaerobic sporing bacilli, including toxigenic strains of Clostridium tetani. This plaster hair is considered to have been the original source of the tetanus infection. Toxigenic strains of tetanus and other anaerobic sporing bacteria were isolated from the dust or floor sweepings of various parts of the operating room suite and from specimens of talc. This is thought to have been the result of dissemination of spore-containing dust originally contaminated from the plaster hair. The dissemination was probably brought about by cross currents of air in the operating room and these were produced by exhaust ventilation in the operating room suite. Clostridial strains including toxigenic Cl. tetani were isolated from talc autoclaved at 20 pounds pressure. This imperfect sterilization was considered to have arisen from the tight packing of the powder packets in the sterilizing drum. The contaminated talc (glove powder) was probably the final vehicle whereby tetanus spores reached the patients' wounds. The author makes recommendations on ventilation systems for operating rooms and on the sterilization of talc.

Seasonal Variations in Thyrotoxicosis.—Morgans and Trotter found in a group of patients who were treated with methyl thiouracil and who were under close observation throughout the year that exacerbations of thyrotoxicosis were most frequent in spring and least frequent in autumn. This may be a direct effect of changes in the duration of daylight or an indirect effect of variations in the amount of goitrogenic substances in the diet. The authors point out that in normal persons basal metabolism tends to reach a peak during spring. This may indicate a springtime increase in thyroid activity.

Electric Blanket for Treatment of Rheumatoid Arthritis.—Frankel used an electric blanket as a means of applying heat for long periods and thus produce sustained vasodilatation. The patient's feet, legs and pelvis are well protected with sheets of cotton-wool wrapped about the limbs and body. The electric blanket is next wrapped about the lower half of the patient's body and kept in position with bandages. The blanket is left in position for several weeks, and the patient is taken out of it only for toilet purposes. The temperature between the cotton-wool and the skin is taken every four hours and is kept at 110 to 115 F. This type of application of heat produces vasodilatation with pronounced sweating. The resulting loss of fluid and salt is made up by additional intake. The fluid intake and output and the amount of chloride excreted are recorded. The patients tolerate this treatment well. They perspire profusely. There is slight pyrexia, the temperature varying between 99 and 100 F., and the pulse-rate is slightly increased. The patients find the blanket treatment comforting and are definite about the loss of pain and improvement in the stiffness and increase in the range of movement of the affected joints. In the last eighteen months 14 patients have been treated. There was striking improvement in every case. Although improvement appears to have been maintained, it is impossible to say whether further relapses may occur.

Acta Endocrinologica, Copenhagen

3:1-104 (No. 1) 1949. **Partial Index**

Antagonism Between Adrenotropic Hormone of Hypophysis and Sex Hormones. H. Hase and L. Schindel.—p. 27.
*Effects of Pituitary Adrenocorticotropic Hormone (ACTH) in Case of Chronic Rheumatoid Arthritis. K. Brøchner-Mortensen, J. Georg, C. Hamburger and others.—p. 39.
Effect of Desoxycorticosterone Acetate (DCA) and Sodium Chloride on Blood Pressure and Renal Function. R. Luft and B. Sjögren.—p. 56.
Synthetic Oestrogenic Substances: Comparative Study on Their Effectiveness in Women. A. B. V. Rydén.—p. 71.

Pituitary Adrenocorticotropic Hormone (ACTH) in Chronic Rheumatoid Arthritis.—Brøchner-Mortensen and his collaborators say that as soon as the reports of the effects of Kendall's Compound E and of pituitary adrenocorticotropic hormone (ACTH) in cases of chronic rheumatoid arthritis had reached Denmark, they decided to try the treatment in suitable cases. Although it proved impossible to obtain the preparations from the United States, the authors received from Sweden an ACTH preparation derived from hogs, in an amount sufficient for their first experiments. A woman, aged 53, who had had severe chronic rheumatoid arthritis for 14 years was treated with daily intramuscular injections of ACTH. The doses were gradually increased from 25 mg. to 100 mg. After two injections of 100 mg. the dose was diminished to 75 mg., which was given for five days; she then received 50 mg. daily for four days and finally one injection of 25 mg. Altogether she received 950 mg. in the course of fifteen days. The clinical effects closely resembled those reported by other investigators. The articular swellings, pain and tenderness on motion rapidly diminished. The articular and muscular functions were improved. She could get out of bed, walk without pain and climb stairs unaided. Her appetite improved, and she experienced a feeling of well-being. The blood sedimentation rate decreased, and the total plasma

protein decreased, because of a diminution of the gamma globulins. There was a negative nitrogen balance and an increase in the uric acid concentration in the serum. Hyperglycemia and glycosuria occurred. The serum potassium and sodium decreased. The number of circulating eosinophils decreased. The urinary excretion of 17-ketosteroids, reducing corticoids and glucocorticoids increased six to 15 times. A few days after discontinuation of the treatment the symptoms of the disease reappeared and the laboratory findings were the same as those prior to treatment. Subsequent treatment with testosterone propionate for fourteen days resulted only in an increased output of 17-ketosteroids.

Athena, Rome

15:105-136 (Sept.-Oct.) 1949. **Partial Index**

*Antagonists of Folic Acid (Pteroylglutamic Acid). J. Messerschmitt. —p. 105.

Antagonists of Folic Acid (Pteroylglutamic Acid).—Messerschmitt reports on the mode of action of biologic antagonists, Woods' substitution theory or inhibition by competition, inhibitory index, reversible action of the metabolite-antagonist pair and its limitations, chemistry of folic acid and related compounds, their activity and toxicity. There is no known structural modification of a metabolite which will originate an antagonist. Not all the compounds of analogous structure have an antagonistic action; some possess biologic activity and others have none. The safety margin is narrow. Doses vary with each product. Their actual toxicity does not allow prolonged treatment at the present time. The author reviewed experiments with folic acid antagonists on strains of bacteria which require folic acid as a growth factor, on chicks which were carriers of Rous sarcoma. He reports on the therapeutic utilization of folic acid antagonists, especially 4-aminopteroylglutamic acid in the treatment of acute leukemia, chronic leukemia and some neoplasias. Neoplastic cells proved more sensitive to lack of folic acid and to the antagonists than normal cells. Remissions were more or less complete, sometimes dramatic. White cell count, red cells and the number of platelets became normal. Bone marrow changes were less pronounced than those in the peripheral blood. He advocates the use of those folic acid antagonists which do not produce a sharp and immediate folic acid deficiency. Chemotherapy appears to be useful in the treatment of leukemia and cancer.

Medicina, Buenos Aires

9:317-398 (Oct.) 1949. **Partial Index**

*Suture and Homotransplant of Aorta: I. Technic; Immediate and Late Results: II. Anatomic Study. A. Lanari and O. Croxatto.—p. 317.
*Changes of Volume of Blood After Thoracolumbar Sympathectomy (Smithwick's) in Hypertension. A. C. Taquini and A. Villamil. —p. 352.

Suture and Homotransplant of Aorta.—Lanari and Croxatto experimented on dogs, in two different groups: (1) those in which the aorta was sutured, after having been sectioned, and (2) those in which a segment of the aorta of another dog was grafted. When suture was performed, circulation was maintained without any interruption, whereas, when a graft was used, circulation was interrupted. The authors describe in detail the technic used for suturing the two cut ends of the thoracic aorta, without interrupting the circulation for more than about six minutes. This procedure is recommended for inserting grafts in the thoracic aorta because the maximum time the circulation can be interrupted with safety at this level is 15 minutes; otherwise paraplegia may occur. Arteriography and pressure measurements were used to study the sutures and the grafts of the thoracic aorta at periods which varied between 12 and 15 months after the operation. It was found that the grafts were unchanged. Aneurysms were found in the dog which lived 15 months after suture of the ends of the resected aorta. Grafting is preferable to simple suture when the tension at the anastomosis is great. The anatomic study was done on 3 dogs with simple suture and on several dogs with aortic grafts. In cases of simple suture the distensible fibrous tissue which joins both ends accounts for the formation of the aneurysm. In the dogs with grafts coaptation was perfect. The presence of areas of partial necrosis and cellular proliferation in the intima of the grafted segment of the aorta, far from the line of suture, indicates that the graft persists as a living tissue. It is of interest to note the presence of chondrogenesis in the recipient aorta in the region subjected to pressure by clamps during operation. This is probably due to alterations in the adventitial vessels.

Blood Volume After Sympathectomy.—Taquini and Villamil carried on observations on 5 patients with essential hypertension. The patients were between the ages of 31 and 53 years. They were observed before, immediately after and some time after they had a thoracolumbar sympathectomy (Smithwick's technic). The time of circulation, the venous pressure, the extracellular liquid and the total proteins of the blood plasma did not change immediately after operation. The volume of blood greatly increased immediately after the operation. The increase became more obvious later, at periods of observation which varied between 368 and 420 days after operation. The increased volume of blood shows steady dilatation of the splanchnic vascular bed. It is possible that the lack of change of the time of circulation, when it is measured with the triketocholanic acid method, is due to the fact that the zones deprived of the sympathetic nerve do not react to this substance.

Medizinische Klinik, Munich

44:1493-1524 (Nov. 25) 1949. **Partial Index**

Abdominal Examination Under Anesthesia. E. Schliephake and L. Meuwsen.—p. 1499.
Changes in Serum Cholinesterase After Vegetative Stimulation in Allergic Skin Diseases. M. Schoog.—p. 1500.
*Contribution to Etiology of Gangrene of Intestines. E. Knappe.—p. 1503.
*Problem of Treatment with Massive Doses of Digitalis. P. Laurentius. —p. 1506.

Gangrene of Intestines.—According to Knappe, the frequent occurrence of an apparently new disease, the so-called gangrene of intestines or necrotizing enterocolitis, in the province of Saxonia as well as in other regions of Germany during the period 1946 to 1947, was due to solanin and to solanidine. In the majority of the cases the disease started after the patient had eaten a large amount of small, unripe or old, budding potatoes. The incidence of the disease increased in spring and summer. The solanin of the potato and of all the solanaceous plants contains tropeine. Consequently, solanin exerts an effect similar to that of atropine, but somewhat weaker. It is an elective organotropic vagus effect; the point of attack is in the stomach or the upper segments of the intestines. The colon may become involved because of paralysis of the pelvic nerve resulting from a stronger effect of the toxin. Products of decomposition, abnormal processes of putrefaction or other impairment of the intestinal tract may be considered as decisive or eliciting factors. The general diet was poor in fats at that time, and that, too, may have favored the disease. A simple method for demonstrating the solanin or solanidine in the urine or in the feces is described.

Treatment with Massive Doses of Digitalis.—According to Laurentius, the effect of digitalis and the tolerance of the drug depends on the condition of the heart. Absolute arrhythmia requires administration of larger doses of digitalis than in cardiac decompensation. Thirty patients with absolute arrhythmia and auricular fibrillation, depending on combined defect of mitral valve, decompensated hypertonia, cardiac infarction and arteriosclerotic lesions of the myocardium, were given only fruit juices for three days. The resulting decrease in pulse rate was 20 to 25 beats, but a pronounced pulse defect was still present. Then 8 to 12 tablets of 0.8 mg. of verodigen, a digitalis glycoside which is absorbed easily and rapidly and has little cumulative effect, were administered within 24 hours. A definite improvement of the pulse, diminished dyspnea and general improvement were observed by the third day. Treatment was continued with one tablet given eight and then six times in 24 hours and gradually less often until the required and final maintenance dose, half a tablet four times within 24 hours, was reached. Treatment with this dose of the drug must be continued for weeks to prevent recurrences. Fibrillation subsided after the administration of 32 tablets of 0.8 mg. of verodigen, within four and a half days on an average. Latent and manifest edema disappeared simultaneously without the use of diuretics. Improved heart action was manifested by the increase in blood pressure amplitude. Sleep and appetite were improved. Results were as good as those

obtained with strophanthin; oral administration of verodigen makes dispensable the difficult intravenous administration of strophanthin. Verodigen is contraindicated in the absence of decompensation and when the life of the patient is threatened immediately, as in the presence of pulmonary edema. Signs of drug intoxication were not observed in the author's cases.

Nordisk Medicin, Stockholm

42:1817-1850 (Nov. 25) 1949. **Partial Index**

*Indications for Resection in Cancer of Rectum. H. K. Lassen.—p. 1817.
*Importance of Salt and Fluid Administration in Treatment of Uncompensated Heart Disease. F. Heintzelmann.—p. 1829.
Capillary Activity of Rutin. F. R. Mathiesen.—p. 1833.
Postvaccinal Encephalitis. V. Petersen.—p. 1838.
Treatment of Alkaline Incrustations in Bladder. Three Cases. R. Andersen.—p. 1840.

Indications for Resection in Cancer of Rectum.—Lassen says that when the tumor is located 8 cm. or more from the anus, as it seems to be in about half to three fourths of the patients with rectal cancer, he recommends transabdominal resection with end to end anastomosis. If the ends of the intestines can be approximated only by traction, resection must be abandoned in favor of amputation. If there has not been difficulty in intestinal passage before the operation, there is no ground for preceding or simultaneous cecostomy or colostomy. In younger, not weakened patients with the tumor situated from 3 to 8 cm. from the anus abdominoperineal resection with simultaneous temporary iliac anus is preferred; in somewhat older and poor risk patients abdominoperineal amputation is advocated. If the cancer is situated 3 cm. or less from the anus, abdominoperineal amputation is done unless the patient is too old and debilitated. With low tumors in old and weak patients colostomy and secondary perineal amputation are advised, with closure of the part of the rectum lying above the tumor. By the procedures outlined, at least half the patients operated on may expect full continence of the sphincter; disturbance of sexual function will occur in only a few of the male patients.

Salt and Fluid Administration for Uncompensated Heart Disease.—Heintzelmann studied the effect of treatment with diets low in salt and with fluid intake up to 3 liters daily in 30 patients with pronounced heart insufficiency and extensive edema. In most cases there was progressive loss of weight and the more abundant fluid supply caused neither subjective nor objective aggravation. He concludes that a diet containing less than 2 Gm. sodium chloride can be of great value in the treatment of uncompensated heart disorders. Limitation of the fluid intake is made unnecessary, and in some cases an abundant supply of fluid (2 to 3 liters daily) will be of added benefit.

Presse Médicale, Paris

57:1097-1116 (Nov. 30) 1949. **Partial Index**

Rachitogenic Diets. J. Cathala and F. Verliac.—p. 1097.
*Role of Bronchial Lavage in Diagnosis and Treatment of Pulmonary Tuberculosis. C. Gernez-Rieux, A. Breton, P. Delwaulle and A. Sevin.—p. 1101.
Sequelae of Circumsion in Algerian Mohammedans and Their Treatment. L. Sabadini, J. Ducassou and M. Imbert.—p. 1103.

Bronchial Lavage in Pulmonary Tuberculosis.—Gernez-Rieux and co-workers performed 462 tracheobronchoalveolar lavages (Abreu's technic) on 401 patients whose roentgenograms suggested pulmonary tuberculosis but who did not expectorate or whose expectoration proved negative on repeated examination and on culture and inoculation in guinea pigs. Results of bacteriologic examination of the tracheobronchial secretions obtained by lavage were positive on culture and inoculation in 155 instances and on simple examination in 18 (37 per cent) of the cases. Women and children swallow voluntarily materials from the lungs and trachea or expectorate badly. Consequently tracheobronchoalveolar lavage should be performed exclusively in adult male patients. Bronchial lavage yielded positive results in 100 of 203 male patients (49.26 per cent) with abnormal roentgenograms of the chest, whose sputum was negative on repeated examination and in whom Koch's bacillus could not be demonstrated on gastric lavage. One hundred and nine of the 203 patients presented roentgenologic pictures suggestive of pulmonary tuberculosis without cicatrization; bronchial lavage was positive in 83 of the 109 patients (76 per cent). The remaining 94 patients presented roentgenologic pictures suggestive of inactive, cicatricial tuberculosis; bronchial lavage was positive in 17 (18 per cent). Eighty-seven patients with an established diagnosis of pulmonary tuberculosis were treated for several years and were considered cured on clinical, roentgen and bacteriologic examination. Bronchial lavage was positive in 31 of these 87 patients (35.6 per cent). Results of bronchial lavage based on culture and inoculation in guinea pigs demonstrated that the incidence of so-called "closed cases" (in contrast to open tuberculosis) is much lower than it was generally believed. There was not a single accident associated with bronchial lavage in the authors' cases. The method should not be used in patients with hemoptysis, respiratory insufficiency, asthma and heart disorder. It is of considerable aid in the early diagnosis of pulmonary tuberculosis, in therapeutic management, in control of recovery and in prophylaxis.

Riforma Medica, Naples

63:1037-1062 (Oct. 29) 1949. **Partial Index**

*Association of Penicillin and Serum Antitoxin in Therapy of Tetanus: Thirteen Cases. A. Cioni and G. Miano.—p. 1037.

Association of Penicillin and Antitoxin Serum in Tetanus.—Cioni and Miano used antitoxin serum, alone or in association with penicillin therapy, in 14 cases of tetanus. For evaluation of results, the patients, who were between the ages of 12 and 40 years, were divided into two groups, those who had antitoxin serum alone and those who had it in association with penicillin. Antitoxin serum was administered by intramuscular or intravenous route, with a daily dose of 50,000 to 200,000 r for a total dose of 100,000 to 2,200,000 r in two to thirteen consecutive days. Penicillin was given intramuscularly, 50,000 units for each injection every three hours, for a total dose of 2,000,000 to 4,000,000 in ten to thirteen days. The results of the combined antitoxin penicillin therapy were satisfactory. The only patient who died in the group of 7 who had the combined treatment was extremely ill when treatment was started. The drugs in association control the tetanic toxin at the focal point and prevent passage of toxins to the blood.

Wiener klinische Wochenschrift, Vienna

61:799-814 (Nov. 18) 1949

Recent Contributions to Pathologic Histology of Peripheral Vegetative Nervous System with Special Consideration of Neurovascular System. I. Obiditsch-Mayer.—p. 799.
Effect of Tyrothricin In Vitro and in Animal Experiments. F. Friza, H. Holewka and K. Rotter.—p. 801.
Epidemiology of Poliomyelitis. S. Krauter.—p. 803.
*Indications for Sulfonamide Medication in Pneumonia. E. Borkenstein.—p. 806.

Indications for Sulfonamide Medication in Pneumonia.—Borkenstein reports on 200 patients with pneumococcic pneumonia who were admitted to the university clinic in Graz, Austria, from 1944 to 1947. During 1944, all the patients with pneumonia were given sulfathiazole, while in 1947 sulfonamide compounds were administered only to those patients who were admitted before the fifth day of the disease. The mortality rate was much higher in the patients who were given sulfonamide compounds after the fifth day of the disease than in those who were given sulfonamide compounds earlier. The mortality rate of the patients given sulfonamide compounds after the fifth day of the disease was higher than in those whose treatment began after the fifth day of the disease but only with quinine-containing drugs. This may be explained by the severe complications, such as pulmonary abscess and empyema, the occurrence of which depended on the treatment with sulfonamide compounds. Sulfonamide therapy, therefore, is indicated in patients with pneumonia before the fifth day of the disease. Results of treatment with sulfonamide compounds before the fifth day of the disease were more satisfactory in patients with unimpaired resistance than in patients whose resistance was impaired. Sulfonamide therapy, therefore, is contraindicated in patients with low resistance, particularly because of the occurrence of suppurative complications. The treatment of pneumonia with sulfonamide compounds is justified by the good results which are to be expected in those cases in which sulfonamide therapy is indicated.

Book Notices

THE REVIEWS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES AND DO NOT REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED.

Operative Technic in Specialty Surgery. Edited by Warren H. Cole, M.D., F.A.C.S., Professor and Head of the Department of Surgery, University of Illinois College of Medicine, Chicago. Introduction by Allen O. Whipple, M.D., F.A.C.S. Cloth. $16. Pp. 725, with 394 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1949.

The development of surgery as a specialty has proceeded on a scientific basis since the discovery of anesthesia and asepsis. The rapid progress in the art soon created a number of subspecialties dealing with limited systems of the body. These developments were fostered, as it were, in a cyclic fashion and intensified by the separation of the teaching of each subspecialty in the various medical schools. Eventually, there were separate departments teaching surgery, but these were autonomous and not connected with the department of surgery of the medical school. Thus gynecologic surgery was almost completely removed from the training provided most residents in surgery. Urologic surgery is now almost wholly a surgical art, with the relegation of treatment of the common infectious disorders back to the general practitioner and the ubiquitous antibiotics. The treatment of fractures by the general surgeon in large communities, once so common, has now largely been transferred to the orthopedic surgeon. These trends were possibly intensified by the development of the American boards, but are also nurtured by our great teaching institutions.

It is curious, therefore, to see a book on operative technic appearing in two volumes under the subheadings "General Surgery" and "Surgical Specialties." The field of general surgery appears to include wound healing, care of the patient and abdominal surgery. A great many lessons from the recent war have been incorporated into the text. Probably the most fundamental is the recognition of the need for large quantities of whole blood in the severely burned or injured patient and most of all in the patient undergoing prolonged radical surgery. Plastic surgery and amputations have drifted somewhat from the realm of the general surgeon; but both sections reflect the latest advancements in these fields. Parotid tumors and radical neck dissections are still performed by many general surgeons. These subjects are well presented.

Defects and diseases of the abdominal wall and its contents will surely interest all general surgeons. The array of talent providing the various chapters is indeed splendid. Resection of the esophagus with esophageal gastric anastomosis at levels as high as the sternal notch is well presented. Selection of abdominal incisions is carefully portrayed. There is apparent some difference in the management of wound disruptions as it appears on page 352 as compared with that on page 105. Duplications in a single system of surgery are apt to be confusing; the technic of radical groin dissection is presented twice, once by a surgeon and later by a gynecologist.

The section on gastric surgery is especially complete and skilfully illustrated. The Bilroth I operation, though seldom performed, should be in the general surgeon's armamentarium. Vagotomy is included as a new and useful procedure. Its advisability in any gastric ulcer seems doubtful. Both the thoracic and abdominal technics are detailed. Intestinal obstruction is another problem which has yielded to the surgeon's endeavor. The value of intestinal intubation and its correct role is outlined. The infrequency of volvulus reported by the author of this section is puzzling. It appears to be not so uncommon in large hospitals dealing with many problems of an emergent nature.

Surgery of the biliary tract and the pancreas and surgery of the spleen are also in the first volume. The chapter on stricture of the bile duct is instructive. The responsibility of the surgeon in this tragic circumstance cannot be too strongly emphasized. Surgery of the thyroid may undergo new evaluation with the new tool of radioiodine. Portal hypertension and its surgical management represent a field of growing interest.

The volume on the surgical specialties is obviously designed to keep the young surgeon abreast in these fields, although his clinical training may leave him inexperienced. This contains such diverse subjects as reconstructive, thoracic, orthopedic and neurologic surgery. Skilful editing has streamlined the work to a useful compendium. Operative technic does not appear to be a matter which can be taught by didactic training. The introduction to the second volume emphasizes the fact that surgeons undertaking radical operations for cancer must be general surgeons of wide experience. Is it possible for general surgeons to encompass so wide a field? In these two volumes a commendable effort has been made to present something on a few of the technics that every general surgeon should know. Surgeons whose interests lie in any segment of their art will find it profitable to possess these books.

The Red Cross Nurse in Action: 1882-1948. By Portia B. Kernodle. Cloth. $5. Pp. 524, with 16 illustrations. Harper & Brothers, 49 E. 33rd St., New York 16, 1949.

This is a history of the Red Cross Nursing Service from its establishment under Clara Barton's leadership through the postwar year 1948. Original documents, newspaper accounts and personal correspondence from the official records of the organization were drawn on in the preparation of this book. Discussions with Red Cross volunteers and professional field workers, present and former administrators of the nursing service and leaders in nursing organizations in this country and abroad have guided the author in interpretating and evaluating policies and programs of the nursing service. Comprehensive developmental data of this service are presented in statistical tables.

Impersonal historical facts are enlivened by colorful character sketches of Clara Barton, Jane A. Delano, Clara D. Noyes and other outstanding contributors to this branch of the Red Cross organization. Also, adding to the general interest of the book are the accounts of the pioneer work in public health nursing and nursing education attempted by small groups of Red Cross nurses following World War I in Unalaska, the Ozark Mountain regions, the Indian Reservations of Southwestern United States and in Eastern Europe.

As the author points out, the history of the nursing service is a part of the history of the entire Red Cross organization, the social history of American and the history of the nursing profession. As such, it will serve as a valuable reference source for students in either of these fields.

Physiology of the Uterus. By S. R. M. Reynolds, M.A., Ph.D., Staff Member, Physiologist, Department of Embryology, Carnegie Institution of Washington, Baltimore. Second edition. Cloth. $12.50. Pp. 611, with 68 illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 E. 33rd St., New York 16, 1949.

The edition appears ten years after the first one. Physicians who never read the first edition missed learning a great deal about the physiology of the uterus. In the present edition, Reynolds has reviewed practically the entire literature dealing with this subject. He tabulates more than 2,500 references. The author index alone occupies 18 pages. This will give one an idea of the enormous amount of work done by Reynolds in preparation for this book.

There are eight parts to the book: (1) patterns and functions of uterine motility, (2) hormone control of the myometrium, (3) uterine growth, (4) circulation of the uterus, (5) metabolism in the uterus, (6) innervation of the uterus, (7) uterosomatic relationships and (8) the onset of labor. The author proves that, whereas the corpus luteum of gestation is indispensable in the first part of pregnancy in the cat, guinea pig, dog, rat, mouse and rabbit, it is not necessary in the second part of gestation in the cat, guinea pig and dog.

Reynolds shows that, whereas neostigmine provides one with a simple method for diagnosing presumptive pregnancy in women without resorting to laboratory tests, this drug has no effect on the nonpregnant uterus in monkeys. The reason for this is not known, but it throws some doubt on the general validity of the theory of the cholinergic action of estrogen on the uterus.

Reynolds summarizes the evidence of a nicely coordinated group of physiologic and nonphysiologic facts constituting the

principle mechanisms of uterine accommodation of the products of conception. He believes that, in view of the general agreement between the accounts of the activity of the undistended uterus of women and that of pituitary responsiveness of the uterus as described by Knaus, the available evidence supports the conclusion that the reactivity data of Knaus are essentially valid. The author maintains that there seem to be some reason to believe that a substance given off by the uterus at certain times will eventually be obtained.

Evidence is produced to show that there is no single cause for the onset of labor. It seems now that parturition begins as a result of gradual accelerating convergence of a number of factors—structural, humoral, nervous, nutritional and circulatory—which, at a time characteristic for each species and adapted to the morphologic condition present in each, are so associated that they lead to evacuation by the uterus of its contents.

This book should be in the possession of everyone interested in physiology, obstetrics, gynecology and infertility. It is beautifully written and is excellently illustrated. The illustrations are clear and instructive; the type is easy to read; the paper is sturdy, and the book is well bound. Both the author and the publishers should be commended for having produced this excellent book.

Mitchell's Pediatrics and Pediatric Nursing. By Robert A. Lyon, M.D., Associate Professor of Pediatrics, University of Cincinnati, and Elgie M. Wallinger, R.N., B.S., M.A., Director of Nursing, Columbus Children's Hospital, Ohio. With a Chapter on Preventive Pediatrics by Rena M. Gazeway, R.N., B.S., M.A. Third edition. Cloth. $3.75. Pp. 590, with 97 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1949.

This edition of this well known textbook on pediatrics for nurses has much to recommend it as the outstanding book in its field. Its coverage of the subject is particularly complete with greater emphasis placed on the topics of increasing present day interest. The section discussing growth and development of the child is excellent. It covers all aspects of development, including the special senses, psychologic progress and emotions as well as the usual material on physical changes. Then a new chapter deals with the work of the public health nurse in homes and schools and the numerous aspects of her work in relation to disease prevention.

Some discussion is given to every disease of any consequence, so that the nurse is made familiar with but not burdened with the details of a medical text. The clearcut discussions are to the point; treatment is touched on only briefly and is up-to-date with the latest biologic agents.

Other sections of the book acquaint the reader with all nursing and medical diagnostic and treatment procedures in the field of pediatrics. A thorough knowledge of the text should familiarize a nurse with all aspects of child care. The book can be recommended as of value to the physician as well, in that it offers a concise summary of disease topics and mental health.

Handbook of Surgical Urology for Internes, Hospital Corpsmen and Nurses. By Nelse F. Ockerblad, M.D., F.A.C.S., Professor of Clinical Urology, University of Kansas School of Medicine. Cloth. $3. Pp. 189, with 52 illustrations. The Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1949.

In the preface the author states, "This little book has been written with the idea that it would be useful to internes, hospital corpsmen and nurses." In this he has succeeded admirably.

A brief but comprehensive history of urology is given. Knowledge of the modern methods of urologic diagnosis, so important to nurses and orderlies, is presented in a simple manner. Nondiagnostic technic and therapeutic procedures are considered in great detail. Attention is called to the value and importance of proper care of urologic instruments. The preoperative and postoperative care of the urologic patient is presented in a manner that cannot be improved on.

The urologic complications of pregnancy, urology in children and the use of the sulfonamides and antibiotics bring this little volume up-to-date. This book fulfils a long-felt want and can be heartily recommended for the purposes for which it has been written. The printing and illustrations are commendable.

Bananas: Chemistry, Physiology, Technology. By Harry W. von Loesecke, Industrial Specialist, Production and Marketing Administration, United States Department of Agriculture, Washington, D. C. Vol. I, Economic Crops, edited by Z. I. Kertesz. Cloth. $4.50. Pp. 189, with 29 illustrations. Interscience Publishers, Inc., 215 4th Ave., New York 3; 2a Southampton Row, London, W.C.1, 1949.

This book is the first of a series of monographs on the chemistry, physiology and technology of food and food products edited by Kertesz. Most of the publications dealing with bananas have been concerned with the methods of growing the fruit and the economics of production. This volume briefly touches on these topics, but the emphasis is placed on the biochemistry of the fruit and its products.

The first few pages are devoted to the history of the fruit and the growth of the trade. The morphology of the fruit and commercial storage and ripening methods are then described. After an excellent discussion of the chemical changes which occur during the ripening of the banana, the author takes up the problems associated with the transportation of the fruit and gives a short description of fourteen products which are made from bananas. He follows this with a discussion of their nutritive value, indicating the need for much more research in this field, and concludes with a description of the many banana diseases and insect pests which plague the growers and act as a limiting factor in the production of bananas.

The author writes very understandably and makes use of references at the bottom of each page rather than a bibliography at the end of each chapter. There are also many excellent illustrations and diagrams, including a color plate showing the variations in color which the banana undergoes during the ripening process. Although there are many tables of data to which no reference is made in the text, they are self explanatory and do not unduly impede one's progress through the book.

As the author states in the forward, "The volume is not intended as a handbook for those concerned with the raising of bananas. Rather it is for those engaged in fundamental researches, so that such workers may be cognizant of results already accomplished or in progress and better informed of the path ahead." The physician, nutritionist or student desiring a compact reference to work which has been done on the banana will find this book invaluable.

Pavlov: A Biography. By B. P. Babkin. Cloth. $6. Pp. 365, with 8 illustrations. The University of Chicago Press, 5750 Ellis Avenue, Chicago 37; Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W.1; W. J. Gage & Co., Ltd., Toronto 2B, 1949.

Professor Babkin's biography of Pavlov is a fitting tribute to the memory of a great scientist. As the senior surviving pupil, who knew him well for 35 years, and who served as his assistant for ten years in the Institute of Experimental Medicine, Professor Babkin is preeminently qualified for the task of writing the biography of Pavlov. With becoming modesty he warns that, in view of the short time since the death of Pavlov and consequent lack of data as well as lack of perspective, the present volume should be regarded "only as material for a future, more comprehensive biography." However, the present opus is a solid contribution to which the future biographers will have little to add.

The book consists of four parts. Part I comprises the biography proper and Babkin's reminiscences of Pavlov. Parts II, III and IV deal with Pavlov's scientific achievements in the physiology of the cardiovascular, digestive and central nervous systems. The scientific material has been presented in a form comprehensible to any intelligent lay reader.

There is nothing sensational or extraordinary in the life story of this man. It is a story of a scientific worker, not unfamiliar in Tsarist Russia, a story of a man of humble origin struggling against poverty and official indifference and at the same time wholeheartedly devoted to the service of humanity and to high ideals. In many ways Pavlov was fortunate: He had good parents, a sympathetic and a most understanding wife and vigorous health. To these must be added two traits which stamp him as a man of genius, his extraordinary power of concentration and endless capacity for work. He was anything but an inspiring lecturer, he rarely formed friendships among his assistants, and he had few interests outside of his work.

Out of this thoroughly objective, dispassionate recital of the many drab circumstances of his life, there emerges, nevertheless, a portrait of a strong man, of a man wholly devoted to a single task, that of experimental physiology. His laboratory and his experimental work absorbed him completely. He was a good husband, a kind parent and a patriotic citizen, but all these facts played a secondary role in his life. His primary interest was the physiologic experiment. "I am an experimenter from head to foot," he was wont to say. In his political views, Pavlov was a mild liberal. He opposed the Bolshevik Revolution as a step, in his opinion, too radical for Russia, but later not only became reconciled to the "new experiment" but spoke enthusiastically about it. The Bolsheviks literally showered Pavlov with funds, assistants, honors and anything he could wish for. The question of the sincerity of the Bolsheviks apparently did not disturb him; he was gratified with the facts.

The second half of the book is devoted to a brief but adequate discussion of the scientific work of Pavlov. Modern physiology owes to Pavlov the introduction into practice of the method of physiologic surgery and a brilliant demonstration of its validity. The last 34 years of his life (1902 to 1936) Pavlov devoted almost exclusively to the study of functions of the cerebral cortex by the method of conditioned reflexes. He was convinced that a conditioned reflex is an elementary cortical reaction. On this physiologic foundation are built the highest and most refined forms of nervous activity which permit an animal or a man to establish their most complicated relations with the outer world. Babkin stresses that Pavlov's abandonment of the physiology of the gastrointestinal tract for the study of conditional reflexes must not be looked on as "serendipity," as it was a logical outcome of his inductive thinking. Babkin also feels that nothing is further from the truth than the oft-cited statement that Pavlov denied psychology. In 1932 Pavlov expressed the opinion that the most important problem of the present day is "uniting or identifying the physiological with the psychological, the subjective with the objective." What is true is that he was primarily an experimenter and had little use for the construction of conceptual systems except as they could be supported by experimental evidence. Pavlov believed that with the help of the conditioned reflex method he would be able to express the whole behavior of an animal in purely physiologic terms. Babkin feels that it is too early to say whether or not this aim could be attained, because the application of the method is hardly 40 years old.

The biography of a great scientist by a distinguished pupil should find a welcome place in the library of every scientific worker and every educated man.

An Atlas of the Blood and Bone Marrow. By R. Philip Custer, M.D., Director, Laboratories of the Presbyterian Hospital in Philadelphia. Cloth. $15. Pp. 321, with 288 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1949.

This is the first atlas of hematology to recognize and propound the advantages of concomitant use of smears and sections in the study of bone marrow. Liberal use of wise selections from a fund of excellent material enabled the author to demonstrate clearly the complementary manner in which these two technics may be employed. His enviably vast source of pathologic specimens made it possible for the more rare hematologic conditions to be well represented. The book is conveniently organized and lucidly written. Organization follows a clinical pattern, rather than a morphologic or pathologic one, a fact which should encourage clinicians in its use. Discussion of controversial subjects has been largely avoided in the accompanying text; but this has resulted in an occasionally oversimplified presentation, an example of which is myeloid metaplasia. Bibliography has been omitted, except for a bare minimum of particular references.

Although photomicrography does not permit reproduction of minute cytologic detail, it is of advantage because of the preservation of architectural pattern. Although, or perhaps because, the material is unsurpassed, a disproportionately large amount of space has been allotted to hemolytic anemias. Thirty-five pages are so occupied, when only three pages are devoted to the refractory anemias of idiopathic variety and of the types which may accompany such nonhematologic diseases as neoplasms, uremia, endocrine failure and pregnancy. Polycythemia vera, together with its varied complications, is represented by only one bone marrow section.

Despite these minor faults, almost all of which may be a matter of opinion, this is probably by far the best atlas of hematology available today. It should prove to be of value, not only to the accomplished clinical hematologist, but to the internist, general pathologist, general practitioner and medical student as well.

The Thyroid Hormones and Their Action. By G. Mansfeld, M.D., Professor of Physiology, University of Budapest. Translated by Erwin Pulay, M.D. Cloth. 24s. Pp. 157, with 60 illustrations. Frederick Muller, Ltd., 29 Great James St., Bedford Row, London W.C.1, 1949.

The author of this monograph has published a number of papers dealing with the respiratory exchange of isolated tissues as affected by variations in thyroid activity. Based on these studies, Mansfeld in the present monograph proposes the theory that the thyroid gland elaborates multiple hormones, including a "myelotropic hormone," which is concerned in hematopoietic action and which is deficient in pernicious anemia, and two hormones designated as thermothyrins, which exert a depressor effect on tissue oxidation. Unfortunately, the experimental data on which the author constructs his theories are so unconvincing as to leave the reader unimpressed. The naiveté of the author is illustrated by his citation of a patient with Graves's disease who was cured by implantation of thyroid tissue from a normal subject. This case is cited as support of the "thermothyrin deficiency, theory of the etiology of Graves's disease. Although much remains to be learned about the thyroid and its disorders, the present monograph can be said only to confuse the field by irresponsible theorizing without substantial experimental or clinical background.

Physiology of Heat Regulation and the Science of Clothing. Prepared at the Request of the Division of Medical Sciences, National Research Council. Edited by L. H. Newburgh, M.D., Professor of Clinical Investigation, The Medical School, University of Michigan. Cloth. $7.50. Pp. 457, with 78 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1949.

This significant volume is a progress report of the research work on the most efficient and practical methods of protecting man against the extremes of external temperatures such as encountered in the polar regions, in equatorial deserts and at high altitudes in the air. This work, by competent biologists, medical doctors and engineers during the late war, was inaugurated by our Armed Forces. Fifteen authors contribute to the 12 chapters of the report. Each chapter is provided with an extensive bibliography. This valuable report shows how far the extremes of environmental temperatures can be mitigated by scientifically protective covering of man. The studies are being continued by both military and civilian groups.

Garrè-Stich-Bauer, Lehrbuch der Chirurgie. Neubearbeitet von Dr. Rudolf Stich und Dr. Karl-Heinrich Bauer, O. O. Professor der Chirurgie, Direktor der chirurgischen Universitäts-Klinik Heidelberg. Fourteenth and Fifteenth edition. Cloth. 60 marks. Pp. 860, with 601 illustrations. Springer-Verlag, Reichpietschufer 20, Berlin W 35 (British Sektor) 1949.

This edition impresses one as a worthwhile attempt to regain the place formerly occupied by German medical textbooks. The revised volume attempts to cover the entire field of surgery. The work presents limitations that are to be anticipated in a one volume work on surgery. A rather surprising fault is that the illustrations deal particularly with far advanced inoperable lesions. The text is satisfactory throughout except that to some extent it is not up-to-date. In the chapter on stomach surgery there is no reference to vagotomy; in the chapter on liver cirrhosis the Talma operation is advocated and only three lines in small print are given to the portacaval shunts. The authors feel that this last operation requires great skill and that it is generally not successful. The same pessimism is expressed with regard to total pancreatectomy in cancer of the pancreas. The authors apparently are not familiar with the work of Brunschwig.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

REDUCING DIET

To the Editor:—**In an obese male patient aged 50, retired, with recurrent symptoms of precordial distress, the electrocardiogram shows a partial auriculoventricular block. How many calories per day are advisable to cause reduction of his 290 pounds (131.5 Kg.) of weight?**

Louis J. Polskin, M.D., Lakeland, Fla.

ANSWER.—In a weight-reducing program a few simple principles must be strictly observed. Except in cases of gout, a high protein, low carbohydrate, low fat diet that allows about 950 calories daily will achieve a weight loss of 2 to 4 pounds (1.2 to 1.8 Kg.) a week.

Of importance is the replacement of minerals and vitamins lost in reducing diets. The high protein diet is extremely successful and need not be feared, even in cases of malignant hypertension or impending renal failure. To the following diet should be added (1) a liberal and potent source of all vitamins and (2), since this is an acid ash diet, some alkali, preferably sodium free, should be added. Some mineral waters offset the acid but contribute sodium, in the presence of which water and weight are retained.

Loss of weight on such a diet occurs in a staircase pattern. On a low calory diet tissue fat is oxidized, either as such or after reconversion to carbohydrate. The tissue spaces are then occupied by water or interstitial fluid, with greater specific gravity than fat. Accordingly, patients on such a diet may actually gain several pounds of weight for a brief period. However, there soon ensues a change in water-tissue balance, with diuresis, loss of 2 to 4 pounds (0.9 to 2 Kg.) in twenty-four hours, then a period of stabilization followed by further diuresis and loss of weight.

A patient weighing 290 pounds should follow the program outlined until a weight loss of 50 to 60 pounds (22.7 to 27.2 Kg.) has been achieved. Then moderate portions of carbohydrate can be added to stabilize the weight for nine to twelve months, after which time a further reduction in weight may be considered. Obviously, any person on a diet of about 1,000 calories cannot expect to accomplish the usual active day's work, any more than can those on the rice diet. Following is the standard reducing program:

Breakfast:
- Fruit or fruit juice, one ordinary portion
- 1 egg plus 1 egg-white, in any form desired
- ½ slice of toast
- Coffee, either black or with skimmed milk

Luncheon:
- Thin soup optional
- Moderate portion of lean meat, fowl, fish or seafood
- 1 cooked vegetable
- Salad
- Fruit for dessert
- Beverage

Dinner:
- Thin soup optional
- Lean meat, liberal portion
- 2 cooked vegetables or 2 portions of 1 cooked vegetable
- Salad
- Moderate serving of cottage cheese
- Fruit for dessert
- Tea, coffee or skimmed milk

All fruits may be eaten either raw or cooked, or canned, if not in extremely thick syrup.

All vegetables either cooked or raw may be eaten, with the exception of corn, peas, beans such as lima beans, rice and potato.

One rounded teaspoonful of citrocarbonate® (a mixture of granular effervescent salts) in a glass of water should be taken twice daily.

Supplemental vitamins.

Fluids should be restricted.

ACTH IN TREATMENT OF ASTHMA

To the Editor:—**Please comment on the potential value of ACTH in the treatment of asthma.**

M.D., Illinois.

ANSWER.—Some laboratory work and clinical trials are now going on with pituitary adrenocorticotropic hormone (ACTH) and cortisone (and similar substances) in experimental hypersensitivity and clinical allergy. One or more of the following considerations have been the stimulus for the individual investigator: 1. The clinical conditions which ameliorate allergic manifestations are similar to those in rheumatoid arthritis. Among these may be mentioned acute infectious disease, pregnancy, jaundice, surgery and anesthesia. 2. Some investigators have claimed that these hormones produce increased antibody release in sensitized animals; others contend that no such increase results. 3. A few have considered rheumatoid arthritis an allergic phenomenon. At present there is little to substantiate this view. The mere fact that one remedy helps two different manifestations does not constitute proof that both are due to the same basic cause. (For example, epinephrine will help asthma and also shock. Asthma may be caused by allergy, the shock by an entirely different factor). 4. Finally, a new and exciting therapeutic approach is always tried on many diseases, with or without rationale.

Events are moving so rapidly in the field of hormone development that by the time this is published the present status may be altered. As of this writing (Dec. 14, 1949), the known situation is as follows: Both pituitary adrenocorticotropic hormone and cortisone (and perhaps other cortical steroids) appear hopeful from the standpoint of being able to produce relief in allergic manifestations. Most of the work thus far is of too short duration and too fragmentary to justify final statements. If these substances prove to be unquestionably effective, the following limitations must be considered: 1. Injections may have to be given daily. This certainly will not constitute a great improvement in the management of the average allergic person. 2. Material is scarce and may remain scarce indefinitely in the case of pituitary adrenocorticotropic hormone. It is possible that complete synthesis of cortisone may be perfected and the compound may become generally available. 3. Cost is great. The cost of cortisone has been now reduced to $150 per gram. At 100 mg. a day, the cost of such material alone for one month of treatment would be $450. 4. The toxic and particularly the possible remote effects from such treatment are definite deterring considerations. Such effects are more to be feared from pituitary adrenocorticotropic hormone, with which multiple hormonal changes may be involved. The most practical application of these substances against allergy in the near future (if the good results claimed are substantiated) should be their use in emergency situations, such as status asthmaticus and similar conditions in which a temporary effective remedy is of great advantage.

OBLITERATION OF UTERINE CAVITY

To the Editor:—**What is the frequency of obliteration of the uterine cavity following curettage either in the pregnant or nonpregnant uterus?**

H. W. Nottley, M.D., White Plains, N. Y.

ANSWER.—Obliteration of the uterine cavity following curettage either of the pregnant or nonpregnant uterus is rare. Practically all the cases reported have been individual ones, and nearly all have appeared in foreign journals. Recently, J. C. Ahumada (*Bol. Soc. de obstet. y ginec. de Buenos Aires* **28**:394, 1949) reported 2 cases. He reviewed the literature and found a total of 60 published case reports. The most extensive paper on the subject is the one by S. Stamer (*Acta obst. et gyn. Scandinav.* **26**:263, 1946), who collected 24 cases. Undoubtedly, more cases of obliteration of the uterine cavity have occurred than have been reported.

The obliteration may be partial or complete. In the cases of complete obliteration the entire mucosa of the corpus and cervix has been destroyed, whereas in the cases of partial obliteration only the mucosa of the isthmus has been destroyed. The latter type is much more frequent than the former, for it occurred in about 75 per cent of the reported cases. Where information was available, 48 followed scraping of a gravid uterus and only 4 occurred after scraping of a nonpregnant uterus.

The prognosis in the cases of complete obliteration is hopeless, because the condition is irreversible. In these cases there is permanent secondary amenorrhea. However, in the cases of partial obliteration, there occurs every four to six weeks a crisis of severe pain in the lower abdomen and pelvic organs, often associated with fever, nausea, vomiting and abdominal distension. These symptoms subside after four to five days.

The diagnosis is easy if one bears the condition in mind, because passing a uterine sound will reveal the true condition. The ideal treatment is gradual dilatation of the cervical canal. In a few published cases, there was a spontaneous cure of the cervical obstruction, apparently produced by the pressure of the blood which had accumulated in the uterine cavity.

BECK'S PASTE

To the Editor:—**A patient has a tuberculous fistula following a nephrectomy. A small tuberculous lesion in the cortex opened when the kidney was freed for nephrectomy. Years ago Beck's bismuth paste was used for such fistulous tracts. Have you any information about current use of this preparation?**

Montague L. Boyd, M.D., Atlanta, Ga.

ANSWER.—Beck's paste (one part bismuth subnitrate and two parts petrolatum) was developed in 1906 as an aid to roentgen demonstration of the source of suppurating sinus tracts and the extent of abscesses and empyema cavities. It was soon found to be of therapeutic value in such lesions and was used extensively for fifteen to twenty years. Bismuth poisoning was early reported, but in 1916 Beck reviewed the general experience, including 1,800 cases of his own without a fatality. In the same year, he reported a series of 21 urinary fistulas, some of tuberculous origin, with remarkable results following the injection of his paste. By 1919 the paste had been modified to consist of one part bismuth subnitrate and nine parts of petrolatum, with 2 ounces (62 Gm.) of white wax per 10 pounds (4.5 Kg.) of paste. Exact details of preparation and administration were outlined, with special emphasis on exclusion of water or oil from the mixture. Beck emphasized the importance of fundamental surgical principles of diagnosis and treatment, the neglect of which not even his paste could correct. The paste was of little value in nonsuppurating sinuses; in fact, bismuth poisoning was more likely to occur from continued use of the paste after the tract had been sterilized.

In spite of its efficacy under proper conditions, bismuth paste now has been generally discarded because there are safer radiopaque materials for outlining fistulous tracts and antibiotics for treatment. In the case cited streptomycin should be used with later excision of the tract, if necessary and feasible. It is assumed that the tract has been roentgenographically visualized with the use of iodized oil, that bacteriologic studies have been made and that presence of a foreign body has been excluded.

References:

Beck, E. G.: Bismuth Paste in Chronic Sinuses and Empyema: Incorrect Technic as a Cause of Failure in Its Application, J. A. M. A. **67**: 21 (July 1) 1916; The Roentgenologic Study of Empyema Cavities, Correspondence, ibid. **72**: 137 (Jan. 11) 1919; A Report of a Series of Unusual Cases Treated with Bismuth Paste, Surg., Gynec. & Obst. **22**: 507, 1916.

Beck, E. G.: Abstracted, Am. J. Roentgenol. **6**: 299, 1919.

RIGHT HEMIPLEGIA AND LEFT FACIAL PARALYSIS

To the Editor:—**What would be the location of a lesion causing a right hemiplegia accompanied with left facial paralysis and motor aphasia? Could such a lesion be produced by an embolism, or would it be caused by a cerebral hemorrhage or thrombosis? Could a person so affected be considered to have full use of his mental faculties within two weeks after the ictus, or would there be impairment of the sensorium?**

M.D., Costa Rica.

ANSWER.—No single lesion could be expected to produce right hemiplegia with aphasia and left facial paralysis. It would be more likely that the conditions present in such a case would consist of right hemiplegia and left facial weakness, with speech disturbances resulting from involvement of the primary innervation of the speech mechanism, causing dysarthria, rather than aphasia. Such a lesion would probably be in the brain stem on the left side. It could be of various types; an embolism, a thrombosis or a hemorrhage would all be possible. The same type of trouble could also result from injury or from neoplasm. There would not necessarily be any involvement of such a person's mental faculties, although he might have considerable difficulty in expressing himself.

If, on the other hand, the interpretation as stated in the query is correct and the patient does have a right hemiplegia with aphasia and, in addition, left facial paralysis, then he must have two separate lesions. Such lesions could be of various sorts, although multiple cerebral thromboses would be the most likely and the patient might not be in full use of his mental faculties two weeks after the ictus.

KETOSIS

To the Editor:—**Are there any comparative data on the production and consumption of ketone bodies in those suffering from starvation and in those with diabetes mellitus?**

Samuel L. Immerman, M.D., Philadelphia.

ANSWER.—The ketone bodies are formed chiefly if not solely in the liver and represent normal intermediate products in the breakdown of fatty acids. They appear to be readily utilized for the production of energy by the peripheral tissues of both diabetic and nondiabetic subjects. However, in the person with uncontrolled diabetes the rate of production may exceed the rate of utilization, with the result that large amounts appear in the blood and are excreted in the urine. If excessive breakdown of fatty acids continues in the subject with uncontrolled diabetes, ketosis progresses and coma finally results. The exact role played by acetoacetic acid in the production of unconsciousness and accompanying symptoms is a matter of dispute. It is of significance that in the starved nondiabetic subject ketosis does not develop to a degree at all comparable with that in the person with uncontrolled diabetes.

Results of studies in recent years do not support the idea that "fats burn in the flame of carbohydrates." It is now generally believed that carbohydrate is not ketolytic and that utilization of ketone bodies is not dependent on the presence or oxidation of dextrose. On the other hand, carbohydrate is antiketogenic in the true sense of the word, and ketosis occurs when it is lacking. When dextrose is available in adequate amounts from the breakdown of glycogen or protein and can be utilized, it is used. When the supply is inadequate, as in fasting, or its utilization impaired, as in uncontrolled diabetes, fatty acids are oxidized in the liver to form ketone bodies, which are then utilized in the periphery (except in the brain, which apparently uses only dextrose).

TREATMENT OF DIABETES INSIPIDUS

To the Editor:—**Is there any new remedy for diabetes insipidus?**

Thomas Van Urk, M.D., Miami Beach, Fla.

ANSWER.—Patients with diabetes insipidus usually respond dramatically to the administration of extracts of the posterior lobe of the pituitary gland or, more specifically, that fraction which contains the antidiuretic principle (beta-hypophamine). The injection of 0.25 to 0.5 cc. of a solution of beta-hypophamine subcutaneously or intramuscularly (for an adult) two or three times a day usually is effective to a gratifying degree. For long-continued action beta-hypophamine tannate in oil may be given intramuscularly in amounts of 0.5 to 1.0 cc. every twenty-four or forty-eight hours. If beta-hypophamine is not available, posterior lobe pituitary solution (surgical) may be injected subcutaneously or intramuscularly two or three times a day in dosage of 0.25 to 0.5 cc.

Patients with adequate breathing space in the nose and with normal nasal mucosa may often secure relief without hypodermic injections by the use of posterior lobe solution applied on cotton pledgets high up in the nostrils. A more convenient method, and the least expensive of all, is the insufflation of posterior lobe pituitary powder intranasally. In most patients the application of a tiny amount of the powder three or four times a day by means of a small atomizer gives prompt and complete relief. One should establish by appropriate tests that nephritis, diabetes mellitus or other disease is not a factor or that frequent urination is not due to habit, nervousness or drugs.

ACETONE AS A CAUSE OF DERMATITIS

To the Editor:—**Could deleterious effects follow the continued use of acetone U.S.P. to dissolve penicillin in oil from syringes. Are the properties of this compound on contact with the hands similar to those of volatile solvents such as benzol and carbon tetrachloride?**

A. E. Powell, M.D., Madison, Va.

ANSWER.—Acetone is known to be a primary irritant. Dermatitis has been reported following its use as a nail lacquer remover. In industry it is also recognized as a source of industrial dermatitis. It is probably less irritating than benzol but about as irritating as carbon tetrachloride. If acetone is used frequently in the cleaning of syringes, some form of protection for the hands is advisable.

CLEFT PALATE

To the Editor:—**A baby 6 weeks of age has a cleft palate which involves only the uvula and the entire soft palate. Should this be repaired, and, if so, at what age? What will be the harmful effects if it is left unrepaired? Does such an anomaly ordinarily interfere with nursing?**

Ralph L. Cash, M.D., Princeton, Ky.

ANSWER.—It is the consensus among plastic surgeons that cleft palate defects, including those of the soft palate only, should be operated on at the age of about 18 to 20 months. If it is left unrepaired the patient probably will develop typical cleft palate speech. On the other hand, proper closure should afford satisfactory speech provided that adequate speech therapy supplements the surgical treatment. The ability to nurse is sometimes impaired because of the leakage of air through the nose. These children sometimes do better fed with a bottle and a large-holed nipple.

EXPOSURE TO MICA DUST

To the Editor:—Could mica, which is used as a dust on plastic sheeting, act as a skin irritant if the sheeting is used to make such articles as baby pants? Would inhalation of mica dust by the employee cause silicosis?

Sidney E. Lenke, M.D., Brooklyn.

ANSWER.—Mica is any one of several complex silicates of the magnesium-aluminum-potassium type. Chemically, but not physically, mica is somewhat akin to some talcs and some asbestos, although the percentage of accompanying free silica may be lower in mica. In view of the frequently reported damaging action of talc as used in the operating room, it appears possible that any raw skin surfaces on infants could be further irritated by mica dust. However, it seems likely that most of any mica dusted onto plastic surfaces would disappear after the first washing. Physiologically mica is rated as an inert dust, since it produces no proliferative reaction. As to workers exposed to mica dust, the problem may be solved by petrographic analysis to determine its free silica content, if any. Since there are many micas, the free silica content may vary appreciably. If this content is less than 5 per cent, then it is necessary only to maintain a work atmosphere harboring less than 50 million particles per cubic foot of air. Nevertheless, it is not desirable to expose workers to this high tolerance level if lower counts may be procured.

PERONEAL MUSCULAR ATROPHY

To the Editor:—Is there any treatment for familial progressive muscular atrophy? I have under observation a father, aged 46, with a severe muscular atrophy of the intrinsic muscles of the hands and feet. (His father, whom I never met, is said to have had a similar condition.) Two daughters, aged 20 and 17, have this condition to a moderate degree. The third daughter, aged 14, is beginning to show early signs of it. The fourth daughter, aged 7, shows no signs. There are no sons. This seems to be the peroneal muscular atrophy of Charcot-Marie-Tooth. Is there any treatment for this condition in the younger children? What are the possibilities of this condition appearing in the next generation?

M.D., New Jersey.

ANSWER.—The history conforms to the usual description of peroneal muscular atrophy of the neural type and familiarly known as Charcot-Marie-Tooth's disease. It is usually hereditary, and a number of pedigrees of affected families have been published. In some instances only the males are affected, but usually both sexes not only transmit the disease but have evidence of it. Nothing certain is known of the causation, and no treatment will arrest the course of the disorder. It is extremely likely that the disease will appear in succeeding generations. Rehabilitation centers have been established which are competent to give massage and appropriate exercises to help maintain the nutrition of the muscles and to aid the patient in making the best of his disabled extremities.

NONALLERGIC BED CLOTHES

To the Editor:—Can I purchase sheets, blankets and mattresses free of allergy-provoking material?

G. W. Hanna, M.D., Homer City, Pa.

ANSWER.—Cotton fiber used to manufacture sheets does not contain antigenic material. Any filler that might be used during the process of manufacture can be removed by thorough washing. Blankets are a problem primarily for those who are sensitive to wool. Cotton blankets (with no admixture of wool) are available from the Beacon Mfg. Co., 300 West Adams Street, Chicago, or from Pacific Mills, 214 Church Street, New York. An electrically heated sheet (Westinghouse Electric Co.) covered with a cotton blanket should be satisfactory. An electric comforter (Westinghouse Electric Co.) also may be obtained. This does not contain allergenic material and eliminates the need of an additional cotton blanket. A "nonallergenic" mattress is a rubber mattress.

PENDULOUS BREASTS

To the Editor:—I would appreciate an opinion on the use of physical methods for the correction of flabby breasts and of pendulous breasts.

M.D., Illinois.

ANSWER.—The correction of flabby and pendulous breasts is based on the etiologic factors involved. The pendulous or ptosed breast presents itself with an atrophic, normal or hypertrophic gland. In all such instances there is loss of firmness and elasticity in the suspensory apparatus of the breast. Even in otherwise normal young girls there may be a tendency of the breast to hang. Senile involution of the glandular and fatty components of the breasts also cause them to descend. The atrophic inelastic skin cannot adapt itself to the reduced volume of the breast and no longer provides support. Similar factors are responsible for pendulousness after rapid loss of weight, or repeated pregnancies. In pendulous hypertrophic breasts the increased volume distends the skin and suspensory ligaments.

The correction of this condition requires affixation (mastopexy) of the gland to the pectoral muscle, with or without reduction of the gland and removal of the redundant skin. A properly fitted brassiere will relieve the pain and dragging sensation on shoulders and chest, as well as backache. Massage and exercise will serve only to aggravate the condition.

DOWICIDE G

To the Editor:—A patient has asked about the possible toxic effects from working with sodium pentachlorophenol, sold under the trade name of doricide or dowicide G. It is used to arrest the development of bacteria in starch solutions. He reports that the filling that he uses in weaving rugs is soaked in this solution and he handles fillings all day. He wants to know whether there are any toxic effects from handling and from inhalation. He has not noticed any toxic effects to date.

M.D., Maryland.

ANSWER.—The sodium salt of pentachlorophenol is a weed, mold and termite control chemical sold under the trade names dowicide G (Dow Chemical Co.) and santobrite (Monsanto Chemical Co.). According to a technical bulletin (TB-023) issued by the Monsanto Chemical Co., it is irritating to the mucous membranes of the eyes, nose and throat in dust form and may provoke violent sneezing and coughing when inhaled. The bulletin also states that the solid material and 1 per cent or stronger water solutions are irritating to the skin of most persons if contact is prolonged beyond five to ten minutes or if repeated contacts for shorter periods occur. Precautionary measures advised for the preparation and handling of solutions of this material are as follows: Avoid contact with the eyes or face; wear rubber gloves if handling entails prolonged contact; wear respirator or fold gauze pad over the nose and mouth if the chemical causes sneezing or coughing, and wash exposed portions of the body with soap and warm water after handling.

RHEUMATOID ARTHRITIS

To the Editor:—What in your opinion is the most effective up-to-date treatment for rheumatoid arthritis?

C. Annest, M.D., Burley, Idaho.

ANSWER.—While cortisone or pituitary adrenocorticotropic hormone constitute the most effective known treatment for rheumatoid arthritis, neither drug is yet available except for investigative purposes. The presently accepted methods in the treatment of this form of arthritis consist in general measures, including increased rest, relief of pain with acetylsalicylic acid or other salicylates and a diet high in protein and vitamins. Physical therapy in the form of heat and active exercises which can be utilized daily by the patient at home is also of definite value. Deformity of the joints should be prevented by orthopedic measures, chiefly removable plaster splints. In many instances, help along psychotherapeutic lines may constitute an essential part of therapy.

DIAGNOSIS OF HODGKIN'S DISEASE

To the Editor:—Can one make a diagnosis of Hodgkin's disease by marrow biopsy only, or must there be a gland biopsy?

T. T. Monaghan, M.D., Corner Brook, Newfoundland.

ANSWER.—Diagnosis of Hodgkin's disease by marrow puncture only is difficult, if at all possible. Foci of Hodgkin's disease may develop in the bone, and, if the aspirating needle secures a specimen from one of these foci, an expert pathologist might make the diagnosis. In general, a marrow biopsy is not sufficient basis for final diagnosis of Hodgkin's disease and a lymph node biopsy is necessary.

BRONCHIAL MONILIASIS

To the Editor:—A patient suffers from chronic pulmonary tuberculosis (inactive at this time) and has frothy sputum showing large numbers of Monilia albicans. A consultant was of the opinion that the patient has bronchial moniliasis. Are iodides contraindicated in this case? Someone has suggested the use of anti-Monilia serum, but I am told that the serum is not available for general use.

Charles W. Price, M.D., Decatur, Ala.

ANSWER.—The iodides are the only known treatment for systemic moniliasis, although they may not benefit severe conditions. The use of antiserum is still in the experimental stage.